September · October 1961 Vol. 11 No. 5

Ca

A Cancer Journal for Clinicians

Published by the
AMERICAN CANCER SOCIETY, INC.

Ca

A BIMONTHLY MEDICAL JOURNAL
OF THE
AMERICAN CANCER SOCIETY, INC.

EDITOR
ROALD N. GRANT, M.D.

ASSISTANT TO THE EDITOR
Miriam F. Smith

EDITORIAL ASSISTANT
Mary Jane Hill

EDITORIAL COMMITTEE

James P. Cooney, M.D.
Harold S. Diehl, M.D.
Sylvia Frank, Ph.D.
E. Cuyler Hammond, Sc.D.
Daniel Horn, Ph.D.
John F. W. King, M.D.

ADVISORY EDITORS

Paul E. Boyle, D.M.D.
Ulrich Bryner, M.D.
Thomas Carlile, M.D.
Anthony Cipollaro, M.D.
John W. Cline, M.D.
Warren H. Cole, M.D.
Murray M. Copeland, M.D.
Emerson Day, M.D.
Kenneth M. Endicott, M.D.
Frank W. Foote, Jr., M.D.
John S. Hirschboeck, M.D.
Arthur G. James, M.D.
C. Todd Jessell, M.D.
John Lindsey, M.D.
Francis W. Lynch, M.D.
James M. McFadden, M.D.
Harry M. Nelson, M.D.
Walter L. Palmer, M.D.
I. S. Ravdin, M.D.
Wendell G. Scott, M.D.
Danely P. Slaughter, M.D.
Wendell M. Stanley, M.D.
Samuel G. Taylor, III, M.D.
Shields Warren, M.D.
Ashbel C. Williams, M.D.
David A. Wood, M.D.
Robert M. Zollinger, M.D.

MEDICAL ART
Frank John Bulin

PRODUCTION
William Glicksman

CIRCULATION
Russell G. Smith

SEPTEMBER-OCTOBER 1961 VOL. 11, NO. 5

CONTENTS

Carcinoma of the Pancreas, Biliary Tract and Liver: Part II 166
Howard F. Raskin, M.D., Robert D. Moseley, Jr., M.D., Joseph B. Kirsner, M.D., and Walter L. Palmer, M.D.

Fibroadenoma of the Breast 182
Joseph H. Farrow, M.D.

Unproven Methods of Cancer Treatment 191

From Pillar to Post 194

Management of Occult Invasive Cancer in Polypoid Adenomas of the Colon and Rectum: An Interview 195

Cancer of the Breast 197
C. D. Haagensen, M.D.

Now Hear This 202

Cancer Around the World 204

Looking at Cancer 205

Cancer Abstracts At a Glance 207

Feedback—From Reader to Editor 208

Articles in *CA* are indexed in INDEX MEDICUS and some are abstracted in CHEMICAL ABSTRACTS, BIOLOGICAL ABSTRACTS, EXCERPTA MEDICA, ABSTRACTS OF WORLD MEDICINE. Publication does not constitute endorsement by the American Cancer Society.

Address correspondence and manuscripts to

ROALD N. GRANT, M.D., *Editor*
American Cancer Society, Inc.
521 West 57th St.
New York 19, N. Y.

Circulation: over 120,000
Annual Subscription: $2.50
Special bulk rate to organizations other than Divisions subscribing in quantities of 200 or more.

Copyright, 1961, by American Cancer Society, Inc., New York, N. Y.

Carcinoma of the Pancreas, Biliary Tract and Liver

PART II

Howard F. Raskin, M.D., Robert D. Moseley, Jr., M.D., Joseph B. Kirsner, M.D., and Walter L. Palmer, M.D.

WALTER L. PALMER, M.D.

Methods of Examination

GASTRODUODENAL EXAMINATION

Because of the clinical symptomatology, patients with pancreatico-ampullary neoplasms generally will have a gastroduodenal examination during the course of their disease. The retrospective studies which have been reported generally deal with the findings of this type of examination.[2,10,21,27,35]

In approximately 50 per cent of cases of carcinoma of the pancreas, changes will be produced in the duodenum and stomach; retrospective studies have shown that in approximately half of these cases the diagnosis can be made or rendered probable. Small defects and minor displacements of the duodenal bulb or second portion of the duodenum are among the findings most frequently overlooked.[35] Small lesions will as frequently produce roentgen findings as large lesions since the abnormalities are usually due to duodenal wall invasion (Fig. 13) and not to increase in tumor size.[2]

It is for this reason that the pancreatic neoplasms diagnosed by virtue of the production of widening of the duodenal loop (Fig. 14) are rarities, as are those tumors of such size that they displace the stomach anteriorly (Fig. 15). Even were these reliable signs, which they are not, if radiologic diagnosis must wait until an invasive lesion has reached such a size, it will generally be a pathologist's and not a surgeon's radical excision that will remove it.

Extrinsic displacements frequently give no good clue as to the origin of the displacing mass (Figs. 16A, 16B). Only by observation of the finer details of mucosal derangement can earlier diagnosis be obtained. Even here the danger of considering lesions pathognomonic must be avoided. The "reverse 3 sign"[18] or epsilon (ε) sign (Fig. 17C), while probably always indicative of abnormality, is by no means diagnostic of pancreatic carcinoma but may result also from duodenitis or pancreatitis.[60] The impression produced in the duodenal bulb because of the dilated common duct associated with mucosal abnormalities in the second portion of the duodenum is a valuable and relatively reliable sign (Figs. 17A, 17B, 17C).[27] As in many situations in radiologic diagnosis, the presence of several ancillary findings leads more certainly to diagnosis.

The possibility of primary duodenal carcinoma as the cause of roentgen findings in this area also must be men-

From the Departments of Medicine and Radiology, The University of Chicago, Chicago, Illinois.

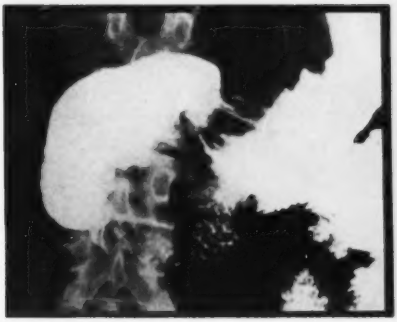


Fig. 13. Woman, 65, with pancreatic adenocarcinoma invading the second and third portions of the duodenum.

Fig. 14. Large pancreatic neoplasm with widening of the duodenal loop.

tioned (Fig. 18). Differentiation may be impossible surgically and difficult pathologically; radiologic separation of such cases from pancreatic neoplastic invasion will certainly not be easier.

Fig. 15. Huge pancreatic tumor diagnosed by anterior displacement of the stomach in the immediate preautopsy period.

Cholecystography

Visualization of the gall bladder by ingestion of opaque materials generally is not of much assistance in the diagnosis of neoplasm of the liver, gall bladder, biliary ducts and pancreas. The presence of the lesion will generally exclude the possibility of gall blad-

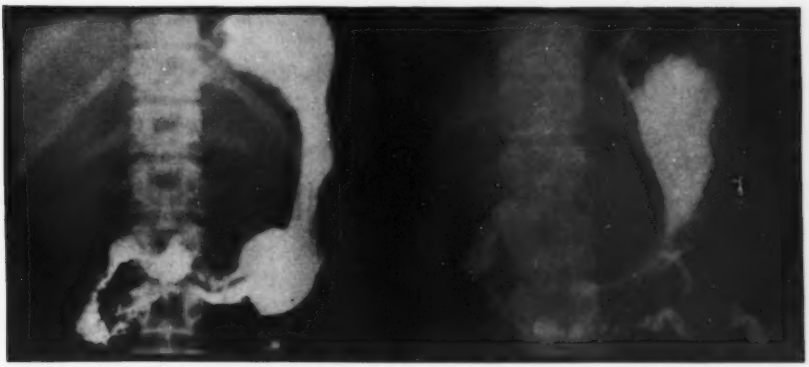
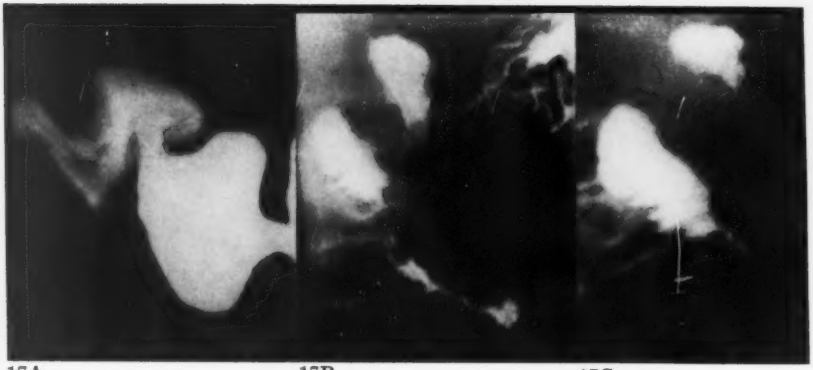


Fig. 16A. Hepatoma causing displacement of the stomach.

Fig. 16B. Carcinoma of the pancreas displacing the stomach.



17A 17B 17C

Fig. 17A. Carcinoma of the head of the pancreas in a 67-year-old male. Note the characteristic deformity of the duodenal bulb.

Fig. 17B. Impression on the bulb caused by greatly distended common duct.
Fig. 17C. Epsilon sign in second portion of duodenum.

der function necessary for visualization. In small polypoid lesions of the gall bladder (Fig. 19), visualization may be accomplished and diagnosis made by failure to effect movement by a change in patient position. Generally, however, these lesions are the result of polypoid cholesterolosis rather than adenomatous polyposis and are probably not even premalignant.

Fig. 18. Primary carcinoma of the duodenal bulb.

Intravenous Cholangiography

The introduction of the hexa-iodo organic compounds (Biligrafin, Cholegrafin),[17,28,29,44] which do not require concentration for visualization of the biliary system, represents a recent forward step in the diagnosis of this area. Unfortunately, though concentration is not required, liver function of sufficient extent is necessary to permit the effective excretion of these compounds. Neo-

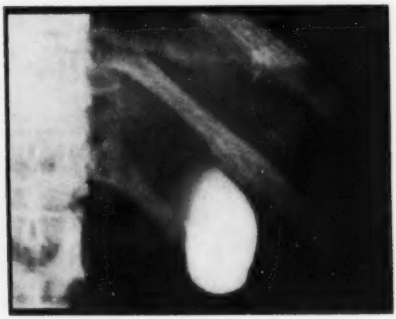


Fig. 19. Polypoid cholesterolosis in a 55-year-old female.

Fig. 20A. Man, 38, was explored because of jaundice with obstructive signs. The common duct was normal at operation; no lesion could be found. Operative cholangiography revealed this massive distention of the intrahepatic bile duct. Further exploration then revealed a carcinoma of the right hepatic duct responsible for partial obstruction.

Fig. 20B. A choledochojejunostomy was performed after removal of the tumor in the right hepatic duct. Postoperative cholangiography shows a return to normal of the intrahepatic ducts (left hepatic radicles not visualized). The patient is well without signs of recurrence two years after surgery.

plastic diseases of the bile ducts or pancreas usually produce obstructive hepatopathy which so decreases liver function that satisfactory excretion is not accomplished. Thus, in the cases in which the information is most needed, the method has the least chance for success.

Premedication with 6 grams of Telepaque and the use of laminography have improved our results and enhanced visualization but, even so, the normal is more diagnostic than the abnormal.

Operative and Postoperative Cholangiography[25,26]

Both of these procedures are utilized primarily to detect stones in the biliary system which can not be detected by probing or by palpation. Tumors may be overlooked at operation as

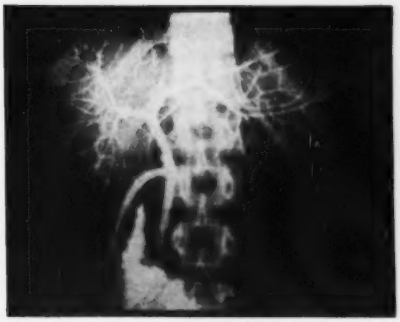


Fig. 21. Normal postoperative cholangiogram with excellent visualization of the intrahepatic ducts.

Fig. 22. Operative cholangiogram with fortuitous visualization of the pancreatic duct system.

Fig. 23. Woman, 52, had obstructive jaundice of acute onset. Percutaneous transhepatic cholangiogram demonstrates the complete obstruction of the markedly dilated common duct. Carcinoma of the head of the pancreas was responsible for the obstruction. Part of the gall bladder is also visualized.

Fig. 24. Man, 62, had a diagnosis of carcinoma of the body and tail of the pancreas established by cytology and by pneumoperitoneal pancreatography (See Fig. 17). Splenoportography demonstrates complete occlusion of the splenic vein due to neoplastic involvement. The tumor mass causes a displacement of the splenic vein in the region of the tail of the pancreas. Collateral circulation is through the vasa brevia. A Levin tube is present in the stomach.

easily or more easily than calculi (Figs. 20A, 20B). These methods thus become very useful in the detection of small, early bile duct lesions.

T-tube cholangiography in the postoperative period (Fig. 21) is particularly helpful in those patients with recurrent jaundice; a normal finding in the asymptomatic postoperative patient is comforting to the surgeon.

Visualization of the pancreatic duct on cholangiograms produced either postoperatively or at operation (Fig. 22) is not unusual. The filling is not indicative of pathology but is an expression of the normal anatomical variations of the sphincter region.

Percutaneous Transhepatic Cholangiography

In cases of poor hepatic function or in the presence of jaundice where even intravenous cholangiography fails to show the biliary structures, a needle may be introduced into the intrahepatic biliary radicles by percutaneous puncture under local anesthesia;[32,43] injection of an opaque organic iodine compound will produce satisfactory visualization of the ducts (Fig. 23).

This method is particularly indicated when simpler methods fail in cases in which the clinical suspicion is biliary tract or pancreatic carcinoma or where the problem is to diagnose the presence of obstructive, as opposed to nonobstructive, jaundice and to determine the site of obstruction.

The chief danger of the procedure is puncture of the extrahepatic biliary system with resultant bile peritonitis. One death has been recorded as a result of this mishap; in our group of only four patients investigated by this technique, there has been one failure of puncture of bile radicles and one case of bile peritonitis. This latter patient had immediate symptoms of shock and the abdomen was explored without delay. A carcinoma of the pancreas was found (this was the cholangiographic

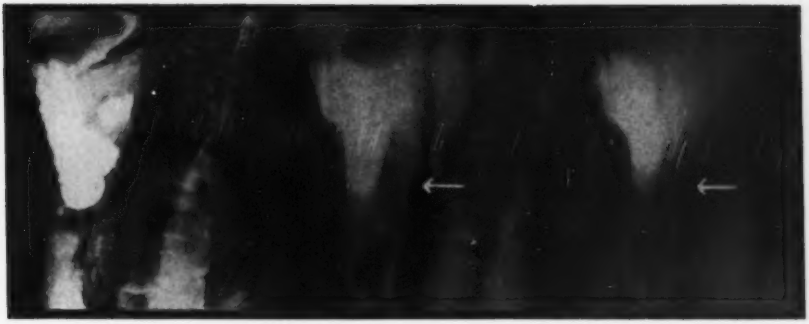


Fig. 25A. Woman, 53, had suspected pancreatic abnormality. Lateral view of abdomen made after the retroperitoneal injection of 1000 cc. of oxygen through the presacral route.

Fig. 25B and 25C. Lateral laminograms made at various levels demonstrate the normal size of the pancreas (arrows). Exploratory operation also revealed a normal pancreas.

diagnosis) and a bypass procedure was performed. The patient died approximately two months later; postmortem examination was refused.

Despite the difficulties and dangers, percutaneous transhepatic cholangiography is of value in the preoperative investigation and diagnosis of pancreatic-ampullary-biliary diseases in carefully selected patients in whom other simpler measures have failed. In the event of technical difficulty, immediate surgical intervention should be available.

Splenoportography

Percutaneous splenoportography[16] is a technically simple, reasonably safe procedure which produces very important information concerning the venous vasculature of the upper abdomen. While it is true that portal hypertension constitutes the primary indication for this procedure, it can also be used with advantage in the investigation of patients with pancreatic neoplasm (Fig. 24). Splenoportal obstruction may be accurately diagnosed and localized preoperatively.

Future experience may indicate the usefulness of splenoportography in the diagnosis of otherwise undetected hepatic metastatic neoplasms.

Pneumoretroperitoneal Pancreatography

By opacifying the stomach and duodenum with orally administered barium sulfate and the retroperitoneal insufflation of air, O_2 or preferably, CO_2 by the presacral route, it is possible to outline the pancreas, to determine its position and size and to detect lesions producing an increase in size of this organ. It is not possible to differentiate benign from malignant lesions and a lesion which does not produce increased pancreatic size cannot be diagnosed by this method.

Laminography[42,63] with the patient in lateral position with the right side down, makes possible differentiation of head, body and tail of pancreas and more accurate localization of lesions.

The normal pancreas is identified just below and posterior to the stomach and duodenum (Figs. 25A, 25B, 25C). The presence of a mass outlined posteriorly by air and anteriorly by the contrast-filled stomach and duodenum

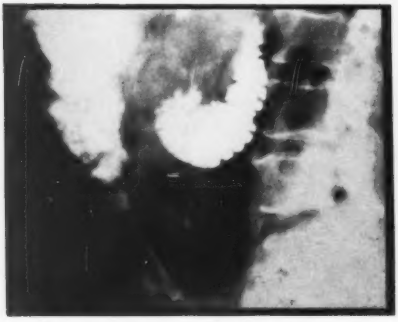


Fig. 26A. (Same case as Fig. 15.) Lateral film of pneumoretroperitoneal pancreatogram showing large mass in pancreas.

Fig. 26B. Laminography demonstrates the position of this mass in the body of the pancreas.

constitutes the diagnostic finding of this method (Figs. 26A, 26B).

Operative Pancreatography and Pancreatic Angiography

Two recently described experimental techniques indicate the future progress to be anticipated in attacking the problem of neoplasms of the pancreas.

Operative pancreatography[13] has the disadvantage that it requires exploratory surgery. Even more forbidding is the fact that the duct of Wirsung must be cannulated by a transduodenal approach, a procedure which is technically difficult and slightly hazardous. However, there are probably occasional indications for the procedure. The difficulty of differentiating grossly, and even on frozen section, between carcinoma and chronic pancreatitis is well known. Certainly opacification of the ducts provides a definite answer to this problem (Fig. 27).

If it were possible to produce this result with an oral intubation method, the accomplishment would represent an important step forward in the management of pancreatic lesions.

Opacification of the arterial vascula-

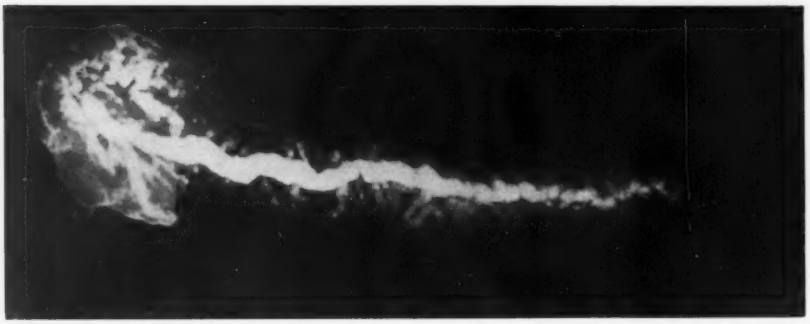


Fig. 27. Injection of operative specimen of total pancreatectomy in a case of chronic pancreatitis with calcifications. Dilated, tortuous ducts are indicative of chronic inflammation. Neoplasm produces localized deformity. No generalized ductal involvement.

ture of the organs under consideration has been frequently accomplished by translumbar aortography.[38,50,51] The selective placing of guided catheters into branches of the abdominal aorta with isolated opacification of the vascular channels[64] is a new method of investigation of the pancreas that holds much promise.

Laboratory Aids in the Early Diagnosis of Pancreatic and Liver Cancer

Carbohydrate Metabolism

As might be expected, a disease process extensively involving the liver, and particularly the pancreas, would impair carbohydrate metabolism quite often. Two per cent of all patients with cancer irrespective of site have diabetes, approximately the expected incidence for the age group. However, 32 per cent of all patients with diabetes and malignancy have cancer of the pancreas.[37] One fourth of patients will have glycosuria or hyperglycemia prior to surgery. The oral glucose tolerance test is a valuable procedure, often reflecting serious disease of the pancreas. Diabetic curves have been reported as often as in 77 per cent of cases, including many patients without glycosuria or elevated fasting blood sugars.

Hypoglycemia with its associated clinical signs is the rarest metabolic disturbance produced by pancreatic neoplasm. The islet-cell adenocarcinomas, composed of beta cells, often quite similar to those of normal islands of Langerhans, may secrete insulin sufficient to produce all the symptoms of insulin shock, including unconsciousness.

Case 6 is that of a young man with a functioning islet tumor who obtained 30 months of relief following surgery.

Case 6 (G.L., #-233821) A 36-year-old clerk had periodic episodes of mental confusion, convulsions and sweating. Hypoglycemia, as low as 16 mg per cent, always accompanied these attacks; therefore, a functioning islet cell tumor of the pancreas was suspected. A 15 cm long tumor composed of islet cells was removed with complete relief of symptoms. Two and one-half years later, the patient was re-explored because of a return of symptoms. A large, functioning, metastatic nodule was found in the left lobe of the liver; a left lobectomy was accomplished but the patient died several hours later.

Enzyme Studies

Serum pancreatic enzymes have been measured for many years, but factors, such as the degree of ductal obstruction and secondary acinar atrophy, are variable influences. Johnson and Bockus, and others[11] have found elevation of serum lipase to be of some value in 40 per cent of cases. An interesting finding of Ross and Klinge is that, while 33 per cent of their 30 patients with carcinoma of the head of the pancreas had elevated serum amylase levels, a surprising 86 per cent (six of seven cases) of ampulla of Vater tumors had elevated amylase levels. The earlier the amylase is measured the more likely will it be abnormally elevated as it decreases to subnormal levels with progression of parenchymatous atrophy. The plasma carotene test has been revised[68] as a screening test for steatorrhea secondary to pancreatic enzyme deficiencies. Five of seven patients with pancreatic malignancy had significantly depressed carotene levels. Blood trypsin levels vary with the status of the pancreas. Because of the presence of an antitryptase in the serum, direct trypsin determinations have been unreliable. Two tests which reflect altered trypsin levels are the plasma antithrombin[39] and Paritol-C[56] determinations. Patients with obstructive jaundice have an increased antithrombin level during the first month, with a gradual fall to subnormal levels after

four months of icterus. The Paritol-C test also purports to measure indirectly an increased level of blood trypsin; results were positive in six of 11 patients. Extensive evaluation of these serologic procedures for early evidence of pancreatic carcinoma is indicated.

A recent addition to the chemical detection of cancer of the liver is the serum glutamic oxalacetic transaminase (SGO-T) activity determination.[71] This enzyme escapes from injured liver cells and subsequent serum levels increase in excess of the normal range of 10 to 40 units. Twenty of 22 patients with metastatic tumor had levels from 40 to 140 units. This test may develop into one of special value for the early diagnosis of liver cancer as there were seven patients in this group who had normal alkaline phosphatases but abnormal SGO-T determinations.

Hepatic Function Tests

There are several easily performed laboratory tests which measure the excretory function of the liver and which may be most suggestive of intrahepatic malignancy when other hepatic diseases are excluded. A persistent, slight elevation of the serum bilirubin, particularly in the absence of clinical icterus, may be the earliest laboratory signal of a malignant process within the liver. One of the most reliable tests is the serum alkaline phosphatase.[41] Significant elevation of alkaline phosphatase secondary to hepatic carcinoma may occur early in the disease, even in the absence of hepatomegaly. An elevated alkaline phosphatase is quite common in obstructive jaundice but this increase probably is not exclusively one of obstruction and retention for several reasons. An elevated alkaline phosphatase can be found in association with normal serum bilirubin; elevations have been noted in both clinical and experimental biliary fistulae in which all the bile drained to the exterior. The liver probably is an important source of the enzyme and injured liver cells contain more phosphatase than normal cells and herein may be a possible solution to this puzzling phenomenon of an increased phosphatase, though the metastases are small.[5] Extrahepatic obstructive jaundice, cirrhosis and bone disease must be excluded when interpreting alkaline phosphatase levels. Probably the most sensitive test available for the detection of minimal alterations in the excretory capacity of the liver is the well-known bromsulphalein dye test. Modest retention of the dye has been noted in liver cancers when serum alkaline phosphatases were borderline or normal and serum bilirubin values were not elevated.

Needle Puncture Biopsy of the Liver

The value of the blind method of needle biopsy of the liver is well established.[67] This procedure has a mortality of only one per thousand, when done properly. A diagnosis of primary or metastatic malignancy can be made in more than 80 per cent of cases. Sometimes, a second biopsy or more will be necessary to establish the diagnosis. An enlarged liver that yields normal liver tissue on biopsy should be suspected of harboring a deep-seated tumor.

Combined Cytologic and Secretory Diagnosis of Pancreatic and Biliary Carcinoma

The diagnosis of these particular cancers could, in many cases, be suspected early, but this is not usually the circumstance. Perhaps it has been the futility of early diagnosis that blocks aggressive and intense diagnostic study. At the University of Chicago,

Table 2

Location of 95 Tumors
and Results of Cytologic and Pancreatic Function Tests

Site	Cytology Negative	Cytology Positive	Abnormal Secretin Test	Both Tests Positive and Abnormal
Pancreas	34	37	43	21
Bile Duct	5	5	1	1
Gall Bladder	6	3	—	—
Duodenal—Primary	0	2	—	—
Duodenal—Metastatic	0	3	—	—
	45	50	44	22

this problem is being approached by a combined study of exfoliative cytology and chemical analysis of pancreatic secretions. Five hundred and fifty-six duodenal drainages have been performed; 95 of these patients have subsequently proven, mainly by surgery, to have a malignancy of the pancreas or biliary system.[47,69]

Thus, the combination of cellular and pancreatic function studies (Table 2) yielded an over-all accuracy of 85 per cent. The demonstration of malignant cells is indisputable evidence of malignancy; a variety of tumors were detected by exfoliative cytology in 50 of 95 cases (53 per cent). Pancreatic bicarbonate and volume determinations were sufficiently abnormal to indicate the presence of severe pancreatic disease (cancer) in another 30 per cent of cases in which all other studies were negative. A rapid flow of pancreatic juice is required to carry malignant cells into the duodenum and this will not occur when the major pancreatic ducts are completely occluded by tumor. Nevertheless, normal pancreatic tissue proximal to the lesion will be stimulated to produce pancreatic juice of normal bicarbonate content, but reduced in volume because of a decrease in functioning parenchyma. The normal response to intravenous secretin is a sharp increase in pancreatic flow, exceeding 1.1 ml per kilogram of body weight for a 30-minute collection period and a bicarbonate level of at least 90 mEq per liter. The most frequent abnormality of the secretin test in carcinoma of the pancreas is a depression of the volume secondary to ductal obstruction. When the tumor is extensive or diffusely infiltrating, then volume and bicarbonate will both be reduced.

Technique of Intubation

Rapid intubation can be achieved by the following method:

1) A Diamond tube is swallowed to the 45 cm mark. The tip of the tube is then in the cardia.

2) The patient lies on his left side on a tilted bench and swallows 15 cm (6 inches) of tubing (Fig. 28).

3) The patient then assumes a sitting position and leans forward as far as possible. Several deep breaths are taken. The tip of the tube slides into the antrum as the anterior gastric wall falls away from the posterior wall (Fig. 29).

4) The patient then lies for five minutes in Trendelenburg position on his right side (Fig. 30).

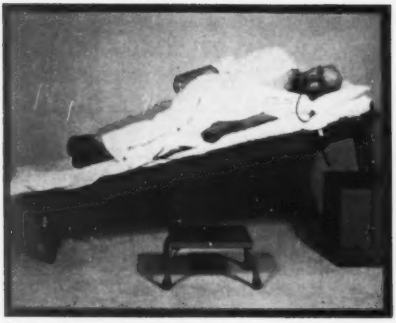


Fig. 28

Fig. 29

Fig. 30

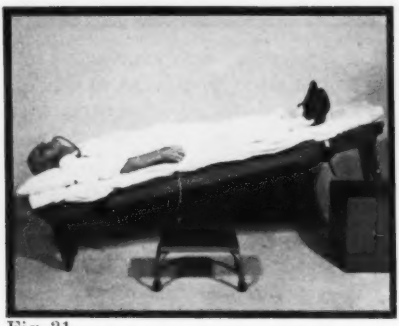


Fig. 31

Figs. 28, 29, 30 and 31. Various positions and maneuvers used during rapid method of duodenal intubation. See text for description.

5) The final position is on the back for three to five minutes. During positions 4 and 5, approximately 10 cm (4 inches) of additional tubing is *slowly* swallowed (Fig. 31).

6) Position of tube is checked fluoroscopically and tip is positioned at proximal end of the third portion of the duodenum. Fig. 32 demonstrates final position of tube in anteroposterior and right lateral views.

When properly performed, the entire intubation can usually be completed in 15 minutes. The stomach and duodenal contents are drained through separate lumens so that the acid gastric contents will not neutralize the alkaline pancreatic secretion. Secretion is given intravenously in a dose of one unit per kilogram of body weight. Three 10-minute specimens are collected. If patient is jaundiced, amyl nitrite is given at the end of the 20-minute collection to increase gall bladder and bile duct flow. Material is centrifuged and sediment is smeared and stained by a modified Papanicolaou technique. The volume of the supernatant is recorded and bicarbonate concentrations are obtained by the Van Slyke method.

At the completion of the pancreatic drainage, both the duodenum and stomach are lavaged for cytologic purposes, as pancreatic tumor will spread occasionally by direct extension through the duodenal or gastric walls.

The combined cytologic and secretory study seems quite logical. Byrnes

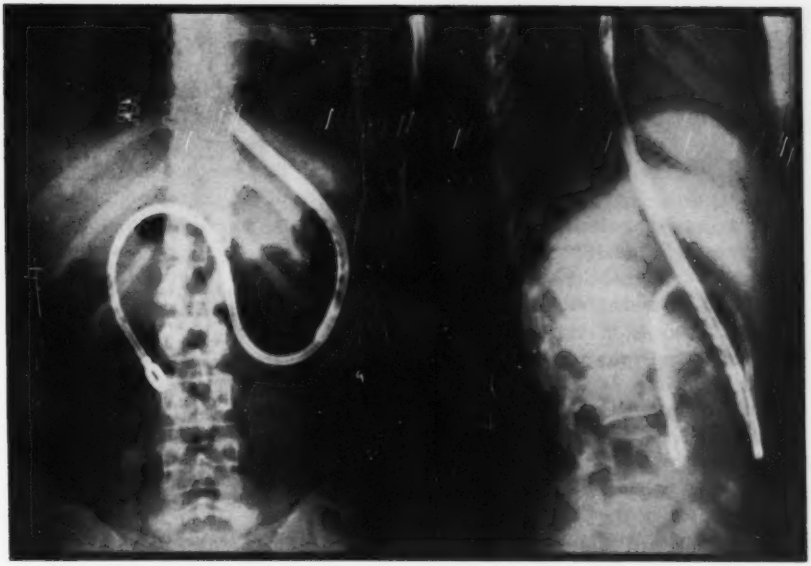


Fig. 32A. Duodenal tube in position for draining. Anterior view. Note that duodenal limb barely crosses in front of vertebral bodies before turning toward the left.

Fig. 32B. Right lateral view demonstrates how the duodenum pursues a posterior course while making its sweep around the head of the pancreas.

and Lemon, in 1954, reported a series of cases of biliary and pancreatic cancers in which they were able to detect cancer in 13 of 36 proven cases (36 per cent); suspicious cells were found in six additional cases. Pollard, Dreiling, and others have studied pancreatic volumes and bicarbonate levels extensively and have been able to detect abnormalities in 40 to 90 per cent of proven pancreatic malignancies. The majority of our cases to date, conforming to experiences elsewhere, have been inoperable, perhaps because intensive diagnostic studies were not begun until after six valuable months of symptoms had elapsed.

Surgery for Pancreatic, Biliary and Hepatic Cancer

The surgical approach to these neoplasms generally has not been effective. Failures are attributable to the insidious early course of the malignant process, the poor physical condition of the patient, the proximity of vital structures and the difficulty of access to the tumor. Success requires superior skill by the surgeon. Tissue diagnosis is imperative, for in the very occasional case one will encounter a lymphoma or Hodgkin's disease for which irradiation or chemotherapy may be helpful The cholemia of obstructive jaundice or secondary atrophy of the pancreas may account for more debilitation than the actual size and extent of the tumor. Carcinomas of the ampulla of Vater have a higher rate of resectability and survival than cancers of the head of the pancreas. The fact that a tumor is palpable should not prohibit surgery, as some pancreatic cancers are entirely within the walls of resectable

cystadenomas. One cannot be absolutely certain of the extent of hepatic involvement by a primary or secondary tumor without direct inspection of the liver.

Radical Surgery

Radical pancreatic surgery was attempted and even temporarily successful in the 1890's. In 1937, Whipple and associates described their two-stage procedure for tumors of the head of the pancreas. The operation has been modified by Brunschwig and others, and consists of en bloc removal of the head of the pancreas, the pyloric end of the stomach and the duodenum. The procedure now is performed in one stage and patients without metastases can remain in fairly normal health. Diabetes does not develop in many and steatorrhea often does not occur in spite of complete loss of external pancreatic secretions. Resection of tumors of the body and tail are less complicated because the head of the pancreas may be spared.

The surgical procedures for carcinomas of the gall bladder and bile ducts vary somewhat, depending upon the size of the tumor and the location plus the contiguous structures involved. Ductal tumors in the hilum of the liver have been excised and a loop of jejunum anastomosed to the open ends of the hepatic ducts.

Palliation: Local Application of Radioactive Materials

One of the most distressing aspects of inoperable cancer of the pancreas has been the severe protracted abdominal and back pain, often resulting in narcotic addiction. Isotope therapy has been highly effective in reducing the severity of pain. The technique of implanting calculated amounts of radioactive material into tumor has been ingeniously applied to the pancreas by Harper and Lathrop. A polyethylene tube is threaded through and around the tumor and radioactive iodine is injected through the tubing. The ends of the tube are sealed and buried beneath the skin. This method is only palliative; several patients examined subsequently at autopsy have been found to have had marked destruction of the tumor adjacent to the implant.

Hepatic Surgery

Partial hepatectomy for neoplasia was reported as early as 1897; by 1951, a total of 16 cases was recorded, six surviving three to seven years. Recently, Pack has revived interest in the problem of hepatic resections and has accumulated a series with promising results. Two mistakes are occasionally made by surgeons on encountering nodules in the liver. Occasionally resectable lesions of the intestinal tract are considered inoperable because of the presence of nodules or lumps seen or palpated in the liver. These are assumed to be metastatic foci and hence the abdomen is closed when in reality only benign cysts, fibromas, or hemangiomas of the liver were present. All suspicious nodules demand a frozen section biopsy. The presence of one or two small peripheral carcinomatous nodules does not necessarily justify the assumption that more are present within the substance of the liver. Sometimes this surmise is incorrect and if local excision or partial hepatectomy had been carried out, a cancer cure might well have been achieved.

One entire lobe and a portion of the other have been safely excised; the procedure in experienced hands requires only 20 minutes to a half hour. Several patients have had "second look" explorations, at which time the regenerative ability of the liver was observed; in a

year there was regrowth of healthy liver tissue equal to the mass of the extirpated lobe.

Case 7 is an example of a re ection of large liver metastatic nodules removed successfully together with the primary lesion.

CASE 7—(W.S., #-626528) A 36-year-old housewife was operated upon for a carcinoma of the rectosigmoid. The lesion was resectable. A large, solitary, metastatic nodule was palpated in the right lobe; the base of the gall bladder was involved. A partial resection of the right lobe of the liver and gall bladder was done. Nine months later the patient has no evidence of recurrent tumor in the liver but, unfortunately, has developed a metastatic lesion in the seventh thoracic vertebra.

Conclusion

The "early" diagnosis of carcinoma of the pancreas, liver and biliary tract thus continues to represent an almost unattainable ideal. The long asymptomatic period and the inaccessibility of these structures to available methods present great obstacles in diagnosis. Recent experience suggests, however, that comprehensive examinations with newer roentgen techniques, chemical analysis and exfoliative cytologic study of the duodenal and pancreatic contents may facilitate earlier recognition of these tumors than had been possible heretofore. Continued investigation of the problem may produce more effective diagnostic techniques. It is conceivable also that as the surgeons deal with more limited neoplasms of the pancreas and biliary tract new procedures and operative techniques will be developed to improve the surgical results and to increase the number of survivors; at least this has been the history of medical diagnosis and surgical management of other previously "incurable" lesions. The early diagnosis and treatment of neoplasms of this region represent one of the most challenging of all cancer problems. The solution to this important problem may depend upon the magnitude of the attention and study directed to it. The objective today may seem unattainable but in relation to the medical and surgical accomplishments noted within our lifetime, the solution should not be discarded as impossible.

References

1. *Abeatici, S. and Campi, L.: Sur les possibilités de l'angiographie hepatique—la visualisation du système portal (researches experimentales). Acta Radiol. 36:383-392, 1951.*

2. *Beeler, J. W., and Kirklin, B. R.: Roentgenologic findings accompanying carcinoma of the pancreas. Am. J. Roentgenol. 67:576-584, 1952.*

3. *Berk, J. E.: Diagnosis of carcinoma of the pancreas. Arch. Int. Med. 68:525-559, 1941.*

4. *Berk, J. E., and Lieber, M. M.: Primary carcinoma of the liver in hemochromatosis. Am. J. M. Sc. 202:708-714, 1941.*

5. *Brinkhous, K. M.: Plasma prothrombin; vitamin K. Medicine 19:329-416, 1940.*

6. *Brunschwig, A.: Radical Surgery in Advanced Abdominal Cancer. Cambridge, University of Chicago Press, 1947.*

7. *Burgerman, A.; Baggenstoss, A. H., and Cain, J. C.: Primary malignant neoplasms of the duodenum excluding the papilla of Vater; a clinicopathologic study of 31 cases. Gastroenterology 30: 421-431, 1956.*

8. *Burnes, W. W., and Leman, H. M.: The cytologic diagnosis of cancer of the pancreas and biliary tract. Transactions Second Annual Meeting, Inter-Society Cytology Council, November 12-14, 1954. Boston.*

9. *Carter, R. F., and Saypol, G. M.: Trans-abdominal cholangiography. J. A. M. A. 148:253-258, 1952.*

10. *Case, J. T.: Roentgenology of pancreatic disease. Am. J. Roentgenol. 44:485-518, 1940.*

11. *Comfort, M. W., and Osterberg, A. E.: The value of the concentration of serum amylase and serum lipase in the diagnosis of disease of the pancreas. Proc. Staff Meet. Mayo Clin. 15:427-432, 1940.*

12. *DaCosta, J. M.: Cancer of the pancreas. [Report] North Am. Chir. Rev. 2:883-909, 1858.*

13. *Doubilet, H.; Poppel, M. H., and Mulholland, J. H.: Pancreatography. Radiology 64:325-339, 1955.*

14. *Dreiling, D. A.: Studies in pancreatic function. IV. The use of the secretin test in the diagnosis of tumors in and about the pancreas. Gastroenterology 18:184-196, 1951.*

References continued from p. 179

15. Eusterman, G. B., and Wilbur, D. L.: Primary malignant neoplasm of the pancreas; a clinical study of 88 cases without jaundice. South. M. J. 26:875-883, 1933.

16. Figley, M. M.: Fry, W. J.; Orebaugh, J. E., and Pollard, H. M.: Percutaneous splenoportography. Gastroenterology 28:153-162, 1955.

17. Frommhold, W.: Ein neuartiges Kontrastmittel für die intravenöse Cholezystographie. Fortschr. Geb. Röntgenstrahlen 79:283-291, 1953.

18. Frostberg, N.: Characteristic duodenal deformity in cases of different kinds of pericaterial enlargement of pancreas. Acta radiol. 19:164-173, 1938.

19. Gerhardt, P. R., and Handy, V. H.: The Ninth Annual Meeting of the Coordinators of Cancer Teaching. Detroit, Michigan, June 3, 1956.

20. Gershon-Cohen, J., and McClendon, J. F.: Oral hepatosplenography; some limitations of iodinated, chloriodized and bromiodized oils homogenized with various emulsifiers. Am. J. Roentgenol. 72: 795-800, 1954.

21. Goldenberg, I. S.: Carcinoma of the biliary tract. Am. J. Surg. 86:292-300, 1953.

22. Gresham, G. A.: Carcinoma of the pancreas; some unusual manifestations. Am. J. Digest. Dis. 1:261-269, 1956.

23. Gustafson, E. G.: An analysis of 62 cases of primary carcinoma of the liver based on 24,400 necropsies at Bellevue hospital. Ann. Int. Med. 111:889-900, 1937.

24. Harper, P. V., and Lathrop, K. A.: Isotope therapy for carcinoma of the pancreas. In: Surgical Forum Proceedings of the Forum Sessions Fortieth Clinical Congress of the American College of Surgeons, Atlantic City, N. J., November 1954. Philadelphia-London, W. B. Saunders Company, 1955.

25. Hicken, N. F.; McAllister, A. J.; Franz, B., and Crowder, E.: Technic indications and value of postoperative cholangiography. Arch. Surg. 60: 1102-1113, 1950.

26. Hight, D., and Lingley, J. R.: The value of cholangiograms during biliary-tract surgery. New England J. Med. 246:761-765, 1952.

27. Hodes, P. J.; Pendergrass, E. P., and Winston, N. J.: Pancreatic, ductal, and Vaterian neoplasms; their roentgen manifestations. Radiology 62:1-15, 1954.

28. Hornykiewytsch, T., and Stender, H. S.: Intravenöse Cholangiographie. Fortschr. Geb. Röntgenstrahlen 79:292-309, 1953.

29. Huber, K., and Stössel, H. U.: Die intravenöse Cholangiographie mit Biligrafin. Schweiz. med. Wchnschr. 84:117-118, 1954.

30. Innerfield, I., and Angrist, A.: Plasma antithrombin determination; new test for cancer of pancreas associated with jaundice. Am. J. M. Sc. 223:422-428, 1952.

31. Johnson, T. A., and Rockus, H. L.: Diagnostic significance of determination of serum lipase. Arch. Int. Med. 66:62-77, 1940.

32. Kidd, H. A.: Percutaneous transhepatic cholangiography. Arch. Surg. 72:262-268, 1956.

33. Kiefer, E. D.: Carcinoma of the pancreas. Arch. Int. Med. 40:1-29, 1927.

34. Kirshbaum, J. D., and Kozoll, D. D.: Carcinoma of the gall bladder and extrahepatic bile ducts; a clinical and pathological study of 117 cases in 15,330 necropsies. Surg., Gynec. and Obst. 73:740-754, 1941.

35. Larsen, K. A., and Pedersen, A.: Roentgenologic findings in the stomach and duodenum in cancer of the pancreas. Acta radiol. 45:459-469, 1956.

36. Leach, W. B.: Carcinoma of the pancreas; a clinical and pathologic analysis of thirty-nine autopsied cases. Am. J. Path. 26:333-347, 1950.

37. McKittrick, L. S., and Root, H. F.: Diabetic Surgery. Philadelphia. Lea & Febiger. 1948.

38. Milanés, B.; McCook, J., and Hernández, A. L.: Aortography and tumors of liver; preliminary report. Angiology 4:312-320, 1953.

39. Mohardt, J. H.: Carcinoma of the gall bladder Internat. Abstr. Surg. In: Surg., Gynec. & Obst. 69:440-451, 1939.

40. Moore, G. E., and Bridenbaugh, R. B.: Roentgen demonstration of the venous circulation in the liver; portal venography. Radiology 57:685-689, 1951.

41. Morey, D. A., and Means, R. L.: Diagnosis of hepatic malignancy; correlation of biopsy, clinical, and biochemical findings. South. M. J. 48:1242-1245, 1955.

42. Moseley, R. D., Jr.: Diagnosis of tumors of the pancreas with the aid of pneumoretroperitoneal pancreatography and splenoportography. Am. J. Roentgenol. 80:967-977, 1958.

43. Nurick, A. W.; Patey, D. H., and Whiteside, C. G.: Percutaneous transhepatic cholangiography in the diagnosis of obstructive jaundice. Brit. J. Surg. 41:27-30, 1953.

44. Orloff, T. L.; Sklaroff, D. M.; Cohn, E. M., and Gershon-Cohen, J.: Intravenous choledochography with a new contrast medium, "cholografin". Radiology 62:868-870, 1954.

45. Pack, G. T., and Brasfield, R. D.: Metastatic cancer of the liver; the clinical problem and its management. Am. J. Surg. 90:704-716, 1955.

46. Pollard, H. M.; Miller, L., and Brewer, W. A.: Clinical study of secretin test. Am. J. Digest. Dis. 9:68-73, 1942.

47. Raskin, H. F.; Wenger, J.; Sklar, M.; Pleticka, S., and Yarema, W.: The diagnosis of cancer of the pancreas, biliary tract, and duodenum by combined cytologic and secretory methods. I. Exfoliative cytology and a description of a rapid method of duodenal intubation. Gastroenterology 34:996-1008, 1958.

48. Richman, S., and Barry, W. F., Jr.: Localized bulge of the right diaphragm simulating neoplasm. Am. J. Roentgenol. 72:122-28, 1954.

49. Rigler, L. G.: Roentgen examination of the liver. [Editorial] Radiology 65:936-938, 1955.

50. Rigler, L. G., and Olfelt, P. C.: Abdominal aortography for the roentgen demonstration of the liver and spleen. Am. J. Roentgenol. 72:586-596, 1954.

51. Rigler, L. G.; Olfelt, P. C., and Krumbach, R. W.: Roentgen hepatography by injection of a contrast medium into the aorta. Radiology 60:363-367, 1953.

52. Ross, C. A., and Klinge, F. W.: Pain and hyperamylasemia as early signs of carcinoma of the head of the pancreas and of the ampulla of Vater. Gastroenterology 12:204-208, 1949.

53. Sansone, G.: Macarini, N., and Oliva, L.: Nouvelle méthode d'exploration radiologique du pancreas chez l'enfant. J. radiol. et électrol. 32:726-733, 1951.

54. Shapiro, P. F., and Lifvendahl, R. A.: Tumors of the extrahepatic bile-ducts. Ann. Surg. 94:61-79, 1931.

55. Shapiro, R.: An experimental study of zirconium compounds in contrast radiography. Radiology 65:429-431, 1955.

56. Shingleton, W. W.; Anlyan, W. G., and Hart, D.: The diagnosis of pancreatic disorders by certain laboratory procedures. Ann. Surg. 136:578-584, 1952.

57. Sproul, E. E.: Carcinoma and venous thrombosis; the frequency of association of carcinoma in the body or tail of the pancreas with multiple venous thrombosis. Am. J. Cancer 34:566-585, 1938.

58. Steinbach, H. L.; Bierman, H. R.; Miller, E. R., and Wass, W. A.: Percutaneous transhepatic portal venography; a preliminary report. Radiology 60:368-374, 1953.

59. Steiner, P. E.: An evaluation of the cancer problem. Cancer Res. 12:455-464, 1952.

60. Stiennon, O. A.: The anatomical basis for the epsilon sign of Frostberg. Am. J. Roentgenol. 75: 282-290, 1956.

61. Stirrett, L. A.; Yuhl, E. T., and Libby, R. L.: The hepatic radioactivity survey. Radiology 61: 930-935, 1953.

62. Stirrett, L. A.; Yuhl, E. T., and Libby, R. L.: A new technique for the diagnosis of carcinoma metastatic to the liver. Surg., Gynec. & Obst. 96: 210-214, 1953.

63. Thomas, S. F.; Henry, G. W., and Kaplan, H. S.: Hepatolienography; past, present, and future. Radiology 57:669-683, 1951.

64. Tillander, H.: Selective angiography of the abdominal aorta with a guided catheter. Acta radiol. 45:21-26, 1956.

65. Vallebona, A.: Récents progrès dans le domaine de la stratigraphie. Acta radiol. suppl. 116: 175-183, 1954.

66. von Moos, F.: Die Tomographie beim Pneumoretroperitonaeum. Schweiz. med. Wchnschr. 82: 629-632, 1952.

67. Ward, J.; Schiff, L.; Young, P., and Gall, E. A.: Needle biopsy of the liver. IX. Further experiences with malignant neoplasm. Gastroenterology 27:300-306, 1954.

68. Wenger, J.; Kirsner, J. B., and Palmer, W. L.: Blood carotene in steatorrhea and the malabsorptive syndromes. Am. J. Med. 22:373-380, 1957.

69. Wenger, J., and Raskin, H. F.: The diagnosis of cancer of the pancreas, biliary tract, and duodenum by combined cytologic and secretory methods. II. The secretin test. Gastroenterology 34: 1009-1017, 1958.

70. Whipple, A. O.; Parsons, W. B., and Mullins, C. R.: Treatment of carcinoma of ampulla of Vater. Ann. Surg. 102:763-779, 1935.

71. Wróblewski, F., and LaDue, J. S.: Serum glutamic-oxalacetic-transaminase activity as an index of liver-cell injury from cancer; a preliminary report. Cancer 8:1155-1163, 1956.

72. Yaskin, J. C.: Nervous symptoms as earliest manifestations of carcinoma of the pancreas. J.A.M.A. 96:1664-1668, 1931.

Fibroadenoma of the Breast

Joseph H. Farrow, M.D.

Fibroadenomas are benign tumors that are composed of epithelial and fibrous tissues mixed in varied proportions but with the fibrous elements predominating and the epithelial structures playing an essentially passive role. They comprise approximately one fourth of the benign noninflammatory mammary lesions seen at Memorial Center. They first appear shortly after the beginning of ovarian activity and are most common in young adults. The frequency decreases slowly during the thirties and declines sharply at the time of the menopause. Fibroadenomas are relatively rare in the postmenopausal breast. They have a definite tendency to multiplicity; at the time of treatment, simultaneous bilaterality was found in 6.5 per cent, and multiple unilateral lesions were present in 2.2 per cent of the cases which were treated at Memorial Center during the five-year period 1951-1955. Follow-up records are incomplete but it is estimated that nonsimultaneous lesions occur in another 5 per cent. More than one fibroadenoma can therefore be expected in approximately 14 per cent of patients with these lesions.

From the Breast Service, Department of Surgery, Memorial Center for Cancer and Allied Diseases, New York, N. Y.

History

One of the earlier descriptions of fibroadenoma was written by Astley Cooper under the title of "Simple Chronic Tumour of the Breast." Without benefit of microscopic studies, he wrote as follows: "This disease is not of a malignant character, and by no means dangerous to life; it is generally very young people who are attacked by it, and we seldom see it in persons above thirty years of age. I will try to describe, in a familiar manner, the mode in which this disease will be exhibited to you. A young person between the ages of fifteen and thirty, will be brought to you by her parents, on account of a swelling in her breast; when you look at her, you see that she has a perfectly healthy appearance, and, in all probability, is much younger than those who are usually attacked by scirrhous tubercle. Her parents being naturally anxious for their child's safety express their fears of the disease being cancerous; at this you smile, and tell them that cancer does not attack persons of her healthy appearance, or persons so young: upon examining the . . . breast you find an exceedingly movable tumour . . . the size [*of which*] is generally from that of a filbert or walnut

to that of a billiard ball . . . having a lobulated feel, being divided into distinct apartments by septa, producing the same kind of sensation to the fingers as fatty tumours; you have here an opportunity of seeing this kind of tumour, and upon carefully examining it, you will find that the account which I have given you is correct. Well, then, the age, and healthy appearance of the person; the lobulated feel of the tumour . . . will at once point out to you that the disease is not cancerous; which, gentlemen, you may inform the person's parents, and likewise tell them that the disease never will become cancerous. I assure you that this disease is not in the slightest degree of a malignant character, neither is it attended with the least danger." Many may doubt the complete accuracy of Cooper's predictions but none would question his simplicity and humanity.

Following the common use of the microscope, a host of different terms was added to the literature in describing fibroadenoma. Whatever useful purpose this varied nomenclature and synonymous terminology may have served is not known other than it clearly demonstrates the universal need for clinicians and pathologists to speak a common language. Certainly little is to be gained by the continuous renaming of long recognized lesions.

Etiology

The etiologic factors of fibroadenomas are not known. Williams believed that 12 per cent of the fibroadenomas which he observed arose in aberrant breast tissue adjacent to but separate from the mammary gland. His belief suggests an embryonal rest as a precursor of fibroadenoma. On the other hand, completely isolated accessory mammary structures are fairly common but as yet there is no clinical indication that they are particularly susceptible to tumor formation. Whether or not unrecognized embryonal rests within the mammary gland are a factor in the formation of fibroadenomas, there is evidence that stimulus for growth does seem to follow the onset of ovarian activity. Fibroadenomas are either absent or extremely rare in adult male and prepuberal female breasts. Further, they are not only uncommon in postmenopausal patients but, if present, are believed to regress partly or present varying degrees of sclerosis and, occasionally, calcification. There is no evidence to indicate that synthetic hormones, particularly androgens, have any therapeutic value in the treatment of human fibroadenomas.

Symptoms and Physical Findings

Fibroadenomas in the average patient are asymptomatic or the symptoms are so mild that the lesions are usually discovered by accident. Increasing numbers are detected during self or routine physical examinations. The rate of growth varies but as a rule is relatively slow with little perceptible change in size or texture over a period of several months. Occasionally there is a history in middle-aged adults of the lesion remaining stationary over a period of several years.

Clinically, fibroadenomas are palpable as firm, encapsulated masses that are freely movable. Tumors of 1 to 3 cm in diameter are round or ovoid in outline but as the size increases they tend to become nodular and lobulated. Fibroadenomas are found in any part of the mammary gland but are most frequently located in the lateral half, mainly in the upper and outer quadrant. Unless quite large they produce no visible change in the contour of the breast. Skin adherence and significant axillary adenopathy are uniformly ab-

sent. Alterations of the usual homogeneous consistency of fibroadenomas are relatively uncommon but may occur because of cysts, myxomatous change, hemorrhage, infarction, sclerosis and calcification.

Treatment

Surgical excision is the only treatment for fibroadenomas. Since the patients are usually young adults, it is desirable to preserve function and to avoid unsightly scars. The choice of incision depends upon the size of the lesion as well as its location in the breast. The three types of incisions commonly used are: (1) radial, (2) circumareolar and (3) curved. The radial incision is made directly over the lesion and is so commonly used that it requires no special comment. The practical advantages are that (1) it is easily extended and (2) it interferes least with the usual radical mastectomy if frozen sections should demonstrate a malignant lesion.

The circumareolar incision causes minimal scarring and deformity but permits limited exposure. It should be reserved for single and small fibroadenomas which underlie or are located within 2 cm of the areolar margin.

The curved or semicircular incision was introduced by Gaillard Thomas in 1882, and has subsequently been modified by Warren and others. It is usually made at the margin of the breast and is particularly useful for the removal of large lesions located in the lateral and inferior halves of the gland. Multiple unilateral fibroadenomas are easily removed through this incision and several radical incisions are thereby avoided.

Regardless of the type of incision used, one should preserve as much of the subcutaneous fat as possible so as to avoid the deformity that results from the fibrous binding of the skin to the glandular tissue.

Fibroadenomas are encapsulated but the fibrous capsule varies in thickness and in many cases is not easily separated from the surrounding breast tissue. Enucleation by blunt dissection is, therefore, difficult, and incomplete removal may result. Excision by sharp dissection with a narrow margin of tissue is preferable. The defect is closed by approximating the mammary tissue with #00 or #000 plain catgut with or without sutures in the subcutaneous fat. A small drain is inserted for 24 or 48 hours and the skin is closed with interrupted silk sutures. A pressure dressing is applied.

Legends

Fig. 1. Juvenile fibroadenoma. Specimen measuring 14 x 8.5 x 6 cm from a patient, age 13, with regular menses for one year. Asymptomatic enlargement of right breast for four months.

Fig. 2. Solitary fibroadenoma present for two years in a patient, age 43. Slow increase in size. When removed, tumor measured 10 x 8 cm. Lesion firm and composed largely of fibrous tissue.

Fig. 3. Multiple fibroadenomas from right breast of an unmarried, 34-year-old woman. Adjacent breast tissue showed atypical papillomatosis. Previously, five fibroadenomas had been removed from same breast and four from opposite side.

Fig. 4. Fibroadenoma containing numerous cysts. Adjacent breast tissue not remarkable. Painless lesion present for two months in a 22-year-old patient.

Fig. 5. Calcified fibroadenoma. One of three discrete stony-hard fibroadenomas removed from the left breast of a 45-year-old patient. Twenty-one years ago and three years ago, fibroadenomas had been removed from the right breast.

Fig. 6. Fibroadenoma showing extensive mucinous transformation of stroma. Patient, age 25, discovered tumor on self-examination five weeks previously.

Fibroadenomas

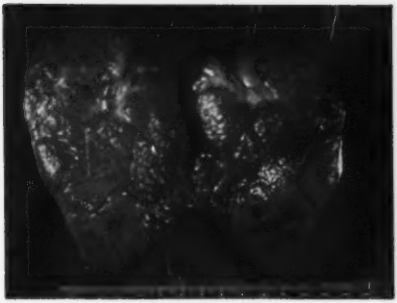


Fig. 1
Juvenile Fibroadenoma

Fig. 2
Solitary Fibroadenoma

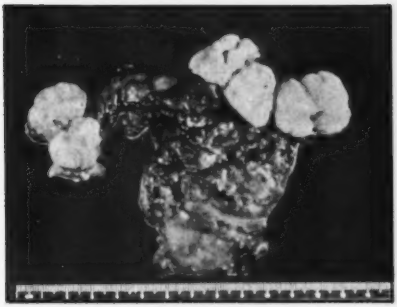


Fig. 3
Multiple Fibroadenoma

Fig. 4
Cystic Fibroadenoma

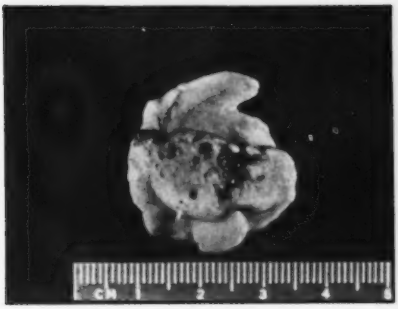


Fig. 5
Calcified Fibroadenoma

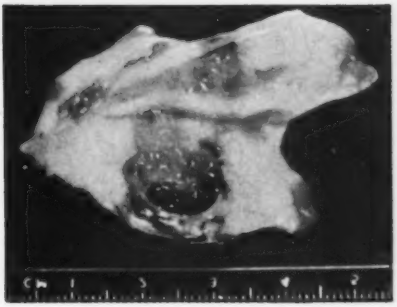


Fig. 6
Mucinous Fibroadenoma

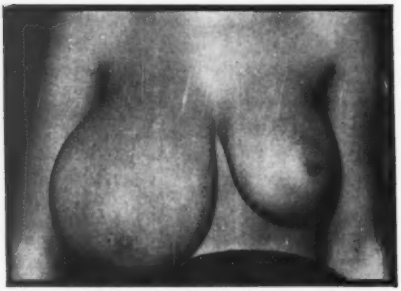


Fig. A. Juvenile fibroadenoma. Age 13. Menses present for three months. Nine months previously breasts relatively same size. Rapid enlargement of the right breast due to a soft encapsulated tumor that measured 20 x 15 x 15 cm. Removal through a curved incision.

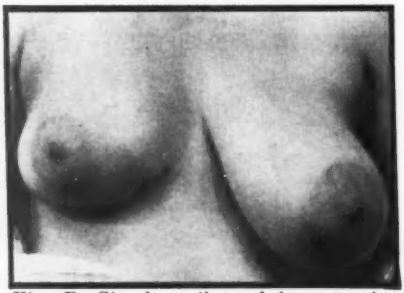


Fig. B. Simple unilateral hypertrophy. Age 15. Menses began at 12 years and since that time progressive disproportionate growth of left breast with nipple and areolar enlargement.

Fig. C. Lactating fibroadenoma occurring in a patient age 20 and six weeks postpartum. Lesion present without noticeable change for six years but grew rapidly during the gravid period. Tumor measured 10 x 8 cm when removed.

Juvenile Fibroadenoma

Roughly 0.5 per cent of the fibroadenomas seen at the Memorial Center are classified as juvenile or fetal. They occur most often within five years after the onset of ovarian activity and in breasts showing more than the average development (Fig. A). Unlike the usual fibroadenoma in adults, juvenile fibroadenomas grow rapidly, are largely composed of epithelial tissues, and may occupy a quadrant or more of the breast at the time of treatment. They are asymptomatic and the patient notices only a unilateral enlargement of the breast. Clinically they are often confused with unilateral hypertrophy of the breast (Fig. B). The latter, like other developmental anomalies, evolves more slowly and in the breast is associated with nipple and areolar development.

Juvenile fibroadenomas are soft, encapsulated and noncystic. Their consistency may differ so little from adjacent mammary tissue that marginal definition is difficult. Prominent and dilated subcutaneous veins over, and adjacent to, the tumor-bearing area are a noteworthy physical finding.

They are treated by surgical excision. These lesions are relatively large and, since they are usually located in the lateral half of the breast, a curved incision is preferred.

Fibroadenoma and Pregnancy

It is fortunate that the problem of simultaneous pregnancy is uncommon despite the frequency of fibroadenomas during the childbearing years. Geschickter and Lewis have published a detailed study of the effect of pregnancy and lactation on fibroadenomas. Although their behavior during the prepartum period is variable, in most instances growth is out of proportion to the surrounding mammary gland.

Following delivery, the epithelium of the fibroadenoma may lactate in an irregular manner and, as a rule, the tumor becomes smaller with postlactation involution (Fig. C). From the limited evidence at hand, there is no appreciable risk of malignant change either in the epithelial or in the fibrous constitutents because of the pregnancy.

In view of these observations, removal of fibroadenomas during the gravid period is based on the uncertainty of diagnosis rather than the need for urgent surgery. In the early months of pregnancy, excision is recommended. During the latter part of the third trimester it may be desirable to postpone surgery until after delivery. If this is the decision, a well-performed aspiration biopsy with a nonmalignant report will do much to relieve the anxiety of all concerned and will warrant the hazards of delay. It is, of course, assumed that the lesion aspirated has the clinical characteristics of a fibroadenoma since a negative aspiration of a poorly defined lesion could lead to false security.

Fibroadenoma and Cancer

Coexisting fibroadenomas are not uncommon in breasts containing mammary cancer. Foote and Stewart in their studies of 300 consecutive cancerous breasts found fibroadenomas in 7 per cent. Carcinoma within a fibroadenoma has been observed but in most instances this was thought to be due to infiltration or secondary invasion from an adjacent primary lesion. Cancer arising within a fibroadenoma is sufficiently rare to warrant citing the following case:

E. C., age 36, mother of two children who were nursed three and four months respectively, was admitted to the Memorial Hospital on February 4, 1940. For one year she had had mild pain and "lumpiness" in the right breast. Physical examination revealed a well-defined, freely movable, 2 cm mass located in the upper and outer quadrant of the breast. There was a soft 1.5 cm lymph node in the adjacent axilla. A clinical diagnosis of fibroadenoma was made and the lesion was excised. Gross examination showed an encapsulated 1.5 cm white nodule with small cysts in the adjacent breast tissue. Microscopic report: Fibroadenoma with noninfiltrating intraductal carcinoma. Without additional treatment there was no evidence of disease during follow-ups extending over 17 years.

Fibroadenoma and Cystosarcoma Phyllodes

In 1838 Johannes Müller introduced the term "cystosarcoma" for certain fibroepithelial tumors which remained stationary or enlarged slowly for a long period and then suddenly and without obvious cause began to grow rapidly, reaching an enormous size in a few months. He believed that these lesions were of an "innocent nature" despite the large size and rapid growth. Müller described three forms: simple, proliferum and phyllodes. Today the term cystosarcoma phyllodes is commonly employed in describing these tumors and usually implies a benign lesion unless otherwise modified. In general, size, stromal cellularity and intracystic proliferations are the most prominent features of cystosarcoma phyllodes. In the benign forms the subepithelial growth may show a wide range of hyperplasia and metaplasia with or without myxomatous changes; only the malignant forms show conspicuous anaplasia. Most benign cystosarcoma phyllodes are encapsulated. In some instances, however, the capsule is poorly defined or may rupture because of expansile growth; there will sometimes be extracapsular extension of the tumor without microscopic evidence of malignant change.

The clinical behavior and microscop-

ic appearance of lesions classified as cystosarcoma phyllodes vary considerably. In an excellent clinicopathological study of 77 cases of cystosarcoma phyllodes from the Memorial Center, Treves and Sunderland found that 41 were benign, 18 borderline and 18 malignant. Their inclusion of a borderline group recognizes the uncertain nature of some of these lesions and the lack of a clear-cut dividing line, clinically or cytologically, between the benign and malignant forms of cystosarcoma phyllodes. Using Treves' and Sunderland's criteria, Lester and Stout reiterated this uncertainty in their review of 58 cases. They state: "With many misgivings and question marks, the group was broken down into 20 histologically malignant tumors, 10 borderline and 28 benign forms." When their studies were limited to the 36 patients treated in the Presbyterian Hospital, only one (2.8%) died of metastases and two had recurrences. Treves and Sunderland in their series reported 10 (12.9%) patients developed metastases.

Although cystosarcoma phyllodes and fibroadenoma are cytologically related, the frequency of the former originating in the latter is not known exactly because of the possible obliteration of a pre-existing lesion by a rapidly growing tumor. Lee and Pack reported, in their study and survey of the literature, that over one half of the cases had a precursory tumor. Treves and Sunderland found microscopic evidence of residual fibroadenoma in 21 of 77 cases. The incidence of benign and malignant cystosarcoma phyllodes among approximately 1,436 fibroepithelial tumors of the breast that were removed at the Presbyterian Hospital was reported as 2.5 per cent by Lester and Stout. A 3.0 per cent incidence was similarly found among approximately 1,100 fibroadenomas treated at the Memorial Center during the five-year period from 1951 to 1955.

The clinical characteristics of cystosarcoma phyllodes vary with the size of the lesion. When small they resemble fibroadenomas and appear as firm, freely movable and encapsulated tumors. As the size increases, they become softer, lobulated and cystic but are still well delineated and mobile. Extremely

Legends

Fig. 7. Benign cystosarcoma phyllodes. Age 38. Lump in left breast for 10 years. Slight increase in size until rapid enlargement during last six months. Lobulated, cystic mass, 12 x 6 x 4.3 cm. Simple mastectomy. No evidence of disease six years later.

Fig. 8. Malignant cystosarcoma phyllodes. Age 31. Lesion present for six years but rapid growth for last six months only. Measured 28 x 10 cm. Simple mastectomy. Six months later, local recurrences and pulmonary metastases. Local X-ray therapy and bilateral oophorectomy. Died of massive pulmonary metastases.

Fig. 9. Benign cystosarcoma phyllodes removed by local excision. Demonstrates intracystic proliferations.

Fig. 10. Recurrent malignant cystosarcoma phyllodes. Age 27. Simple mastectomy at another hospital six months previously was followed by rapid local recurrences. Radical resection followed by local recurrence, pulmonary and liver metastases and death.

Fig. 11. Malignant cystosarcoma phyllodes. Age 45. Tumor present for 10 years. Breast bruised by a fall one year prior to admission, with rapid growth of tumor for past three months. Radical mastectomy with skin graft. Local recurrence 10 months later. Death from pulmonary metastases and secondary deposits in the vertebrae, ribs and sternum.

Fig. 12. Medullary carcinoma demonstrating the physical similarity to cystosarcoma phyllodes. Age 77. Progressive growth of tumor for four years. Radical mastectomy. Surviving five years without evidence of disease.

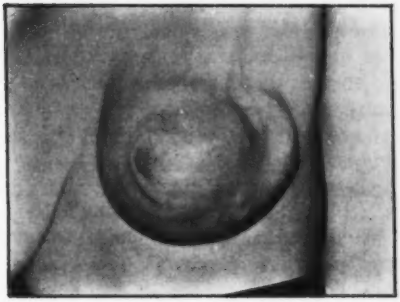


Fig. 7
Benign Cystosarcoma Phyllodes

Fig. 8
Malignant Cystosarcoma

Fig. 9
Benign Cystosarcoma

Fig. 10
Recurrent Malignant Cystosarcoma

Fig. 11
Malignant Cystosarcoma

Fig. 12
Medullary Carcinoma

large tumors are more vascular with marked enlargement of the subcutaneous veins. They are less circumscribed, not uniformly encapsulated, and may fungate, due to pressure necrosis rather than infiltration of the skin. Skin adherence, dimpling, satellite nodules and significant axillary adenopathy are conspicuously absent.

The benign forms of cystosarcoma phyllodes are treated by local excision, provided their size permits a wide margin. A simple mastectomy will obviously be required for large lesions. Borderline and benign recurrent lesions should probably have a simple mastectomy. Despite controversial opinions and with full awareness of the fact that with extremely few exceptions metastases are by the blood stream, I believe malignant forms should be excised by radical mastectomy. While it is true that long-term survivals have been observed following a less radical or even local excision, in other not infrequent instances, local recurrences as well as later distant metastases have appeared. From the evidence at hand, malignant cystosarcoma phyllodes does not respond to X-ray therapy. Hormonal alterations have been so infrequently used that evaluation is not possible.

Summary

Fibroadenomas are benign, slow-growing and encapsulated fibroepithelial tumors with a tendency to multiplicity. They first appear during adolescence and are most often found in young adults. Their etiology is not known although ovarian function seems to be a factor in their growth and persistence. Exceptions to the relatively slow growth are not common but do occur in the juvenile forms, during pregnancy and in those lesions that develop cystosarcoma phyllodes. Alterations of the epithelial constituents within a fibroadenoma may or may not occur in unison with similar changes in the surrounding breast tissue. With extremely few exceptions these alterations are of a benign disposition. The growth variations occurring in the stromal constituents are most important; these give rise to the benign and malignant forms of cystosarcoma phyllodes. Hence, malignant changes within a fibroadenoma are usually sarcomatous and very rarely carcinomatous in nature. Fibroadenomas should be surgically excised.

References

1. *Cooper, A.: Lectures on the Principles and Practice of Surgery. 6th ed. London. Henry Renshaw. 1839; p. 392.*

2. *Foote, F. W., and Stewart, F. W.: Comparative studies of cancerous versus noncancerous breasts. Ann. Surg. 121:6-79, 1945.*

3. *Geschickter, C. F., and Lewis, D.: Pregnancy and lactation changes in fibroadenoma of the breast. Brit. M. J. 1:499-504, 1938.*

4. *Lee, B. J., and Pack, G. T.: Giant intracanalicular myxoma of the breast. Ann. Surg. 93:250-268, 1931.*

5. *Lester, J., and Stout, A.: Cystosarcoma phyllodes. Cancer 7:335-353, 1954.*

6. *Müller, J.: Über den feineren Bau und die Formen der krankhaften Geschwülste. Berlin. G. Reimer. 1938; p. 54.*

7. *Thomas, T. G.: On the removal of benign tumors of the mamma without mutilation of the organ. New York J. Med. 35:337-340, 1882.*

8. *Treves, N., and Sunderland, D. A.: Cystosarcoma phyllodes of the breast; a malignant and a benign tumor. Cancer 4:1286-1332, 1951.*

9. *Warren, J. C.: Plastic resection of the mammary gland. Ann. Surg. 45:801-809, 1907.*

10. *Williams, W. R.: Diseases of the Breast; Their Pathology and Treatment, with Special Reference to Cancer. [Monograph.] London. John Bale & Sons. 1894; pp. 75-76.*

Unproven Methods of Cancer Treatment

The following statement on the Glover Serum, proposed by Thomas J. Glover, M.B., was recently distributed to the 60 divisions of the American Cancer Society for their information. A commentary on the book THE LONG SEARCH FOR THE TRUTH ABOUT CANCER *by Mark Boesch follows.*

The Glover Serum

The Glover serum, according to the American Cancer Society's files, was proposed by Thomas Joseph Glover, M. B., Toronto, Canada, in 1920. Dr. Glover reported that he obtained from blood cultures of many cancer patients and from cancer tissues, a pleomorphic organism that passed through a Berkefeld filter. Variants of this have been secured by animal inoculations and special cultural methods. It has also been referred to as a virus. In preparing the serum, filtrates obtained by passing seven-day cultures of several strains of the microorganism through Berkefeld filters were injected into horses which were later bled. It was reported that only a limited amount of the antiserum was made. The initial dose was 2 ml and subsequent doses of gradually increasing amounts were given at intervals of two or three days, usually near the site of the neoplasm. Charges were reported to be $25 for five doses.

Thomas J. Glover, M. B., was born in Canada in 1887, received an M. B. at the University of Toronto in 1911, and was licensed to practice medicine in Ontario in 1913.

In June, 1920, Dr. Glover demonstrated both the filtrable microorganism and cancer patients who had been treated with the serum before the members of the staff of St. Michael's Hospital in Toronto. When controversy developed as to whether there was any real basis for this work, he voluntarily resigned from the staff, and opened the T. J. Glover Research Laboratories, 538 Jarvis Street, in Toronto.

In 1921, the Murdock Foundation was organized in New York City. This, according to a report published in 1940, was primarily concerned with laboratory research. Mr. J. J. Murdock, who was general manager of the Keith-Albee movie circuit, is said to have supported this organization generously. The Foundation was last mentioned in 1940 when they published an 80-page booklet, "The Treatment of Cancer in Man; Results Obtained in the Treatment of Cancer in Man with a Specific Antiserum," by T. J. Glover, M. B., and J. E. White, M. D. The address of the Foundation at that time was given as 2519 Creston Avenue, New York, N. Y.

On July 9, 1924, Dr. Glover addressed the Philadelphia Clinical Society at the Academy of Natural Sciences. Physicians from the National Stomach Hospital in Philadelphia and from St. Michael's Hospital in Toronto spoke favorably of results obtained with the serum. Other physicians, including Drs. John A. Kolmer, Joseph McFarland and James A. Ewing, expressed scepticism about the work. Newspapers reported the event and the discussion which followed it in detail.

From 1929 to 1938, Dr. J. L. Engle worked with Dr. Glover at the Hygienic Laboratory (now the National Institutes of Health, Bethesda, Maryland), checking Dr. Glover's theories and claimed results in the etiology of cancer. They reported that they produced a malignant tumor in one of a group of guinea pigs that were inject-

ed with the microorganism claimed to have been isolated by Dr. Glover. (*Public Health Reports* 48:319-321, March 31, 1933). Other investigators at the Institute were unable to confirm their results, working independently. Later it was reported:

1. Review of slides of the "tumor" showed a subacute granuloma containing numerous torulus-like organisms.

2. *Cryptococcus neoformans* was isolated from a number of similar "tumors" said to have been produced by the Glover organism, and similar lesions were reproduced in guinea pigs with this organism.

A reference to Dr. Glover in 1959 stated that he was still in practice in Toronto, but had ignored requests for information on his present work. He was regarded as "a very uncommunicative individual, difficult to approach." He no longer published his findings.

Two attempts to evaluate the Glover serum have been reported. In January 1921, a committee, appointed by the Toronto Academy of Medicine the preceding October to investigate the claims of Dr. Glover, reported that Dr. Glover had refused to permit its members to visit his laboratory or to examine his cultures and experimental material. In examination of his claims of clinical benefit in treatment of cancer, the committee examined 12 patients, treated and selected by Dr. Glover, interviewed attendants of these patients, and investigated case reports of patients treated with the serum at St. Michael's Hospital in Toronto. At the conclusion of their investigation, the committee reported that it found no evidence to warrant the hope that a specific cure for cancer had been discovered by Dr. Glover or that the serum had produced a cure in any case definitely established as cancer. (*J.A.M.A.* 76:396, Feb. 5, 1921.)

In 1921, Dr. Francis Carter Wood purchased from Dr. Glover a quantity of serum which he injected into white rats with transplanted carcinomas and sarcomas. Injections were subcutaneous, intramuscular and into the tumors. No beneficial effect of the therapy was found. (*J.A.M.A.* 76:885, March 26, 1921.)

After careful study of the literature and other information available to it, the American Cancer Society has found no evidence that treatment with the Glover serum results in any objective benefit in the treatment of cancer in human beings.

The Long Search for the Truth About Cancer

The first part of the book, The Long Search for the Truth About Cancer, by Mark Boesch, Hamilton, Montana (published by G. P. Putnam's Sons, 1960, $4.95, 307 pp., 147 refs, indexed), is a discussion of the work beginning in the late 1700's, largely unaccepted, of various individuals who believed in the theory of the microorganism etiology of cancer, with the causative agents variously described as bacteria, viruses, or other forms of microorganisms. In tracing this history, the author also discusses various types of treatment for cancer which arose from this concept of the disease, under such chapter headings as: "Early Theories, Experiments, and Discoveries in Cancer," "Virchow and the Cell Theory," "The Rising Science of Bacteriology," "Beginning of a Long Debate," "Coley's Fluid," "Increasing Evidence," "Doyen of Paris," "The Work of Schmidt," "Erwin F. Smith and Plant Cancer," "Rous' Chicken Sarcoma," and "Young of Edinburgh."

The last third of the book, beginning with the chapter, "Scott and Glover," takes up the Glover serum and the lifelong efforts of Michael James Scott, M. D., Seattle, Washington (formerly of Butte, Montana), to secure recognition for this therapy, which he calls the Deaken serum.

According to Mark Boesch in the book, "The Long Search for the Truth About Cancer," the Glover serum was discovered by Tom Deaken, a laboratory assistant, who claimed to have used it with complete success on experimental animals in 1917-18. Fearing medical ridicule, he allowed Dr. Thomas J. Glover, whom he met in 1920, to claim the discovery as his own, hoping in this way to win acceptance of the serum. In 1921, Dr. Scott, a surgeon, hoping to find a treatment other than amputation for cancer of the finger of his left hand, visited the laboratory in New York City where Dr. Glover and Mr. Deaken were working. Although he decided to have his finger amputated, Dr. Scott became convinced that the serum was an effective treatment for cancer, and spent much of the following four years arranging for clinical trials of the preparation by his friends, although he had not learned the method of preparation from Dr. Glover. By 1925, Dr. Scott became convinced that enough medical evidence had been accumulated to make a full medical presentation, but Dr. Glover still refused to divulge the formula or method of preparation of the serum. It was at this time that Tom Deaken told his story to Dr. Scott and broke with Dr. Glover who "went back to Canada." The remainder of the book is concerned with Dr. Scott's efforts to win recognition that the serum is an effective treatment for cancer, and with criticism of organizations interested in cancer research, principally the American Cancer Society, for not granting this recognition. At the time the book went to press, Mr. Deaken had died some time before, and negotiations were being conducted with a laboratory in the East to test the serum.

Not mentioned in the book, however, was the work of Drs. Engle and Glover at the National Institutes of Health from 1929 to 1938, nor the continued interest of the Murdock Foundation resulting in the publication of "The Treatment of Cancer in Man" in 1940. The extensive bibliography fails to include articles by Dr. Glover, *Canada Lancet and Practitioner* 74:92-111, 1930; and by Drs. Engle and Glover, *Public Health Reports* 48:319-321, March 31, 1933, although it does include the review of the report of the Toronto Academy of Medicine in the *J.A.M.A.* 76:396, Feb. 5, 1921.

According to the 1958 A.M.A. Directory, Michael J. Scott, M.D. was born in 1877, and received an M.D. from the Creighton University School of Medicine in Omaha, Nebraska, in 1903. He is a member of the College of Surgeons and is at present retired.

From Pillar to Post

"... The parents of a child with fibrosarcoma had learned of a patient I was treating with 5-Fluorouracil with modest success and came to ask if it would help their child. I replied that to my knowledge and from what I could learn from the work of others that it did not offer promise in such a situation but that I would seek information as to what might offer help when I attended the Conference on Chemotherapy of Solid Tumors at Madison, Wisconsin and the Fourth National Cancer Conference at Minneapolis.

I learned that this family had been advised by a couple of doctors to have the child's leg amputated to halt the disease and one of those doctors was Dr. ____ of your city. Another doctor had advised a perfusion of the limb. Instead, the family had been lured to the use of Krebiozen, although the doctor they had prevailed upon to administer it was doing so without much faith in it or enthusiasm for his task.

This family is intelligent and asked for my opinion. I feel that I have their respect and I should like to give them an honest and intelligent conclusion. I have an opinion but it cannot be very convincing or deserving of great weight because it is based on a paucity of facts. I don't believe I'm much different from most other doctors in this situation except, perhaps, that I have a little more interest in knowing the true facts.

I have tried to guide these people to responsible authorities in cancer treatment. I arranged to have the patient seen by Dr. ____ and he took pathological slides back to the University where he consulted with their pathologist and Dr. ____. The latter proposed that she come there for a groin dissection and a simultaneous limb perfusion, if advisable. In the meantime, the father was in contact with ____ Hospital in N. Y. State and the National Cancer Institute at Bethesda. I also helped to arrange an examination in N. Y. by Dr. ____ and he advised that she be treated here locally with Actinomycin D and mentioned Dr. ____, the co-winner of the Nobel Prize of a few years ago, as one who could give that drug. Then I contacted Dr. ____ and he saw the father and thought it was arranged to have her treated in the University Hospital here. However, the father felt he owed a little loyalty to Dr. ____, [*the doctor who had suggested Krebiozen*—ED.] and took the child to Chicago in order to allow him a final observation before he started the new treatment.

Dr. ____ persuaded him that Krebiozen was akin to Actinomycin D, and that a horse suffered the toxicity so that the patient was spared the ill effects. Then he informed him that their new Krebiozen was 10 times as potent as the original and persuaded him to allow him to administer a dose while there and proposed a trial of at least a month more. The father came asking me to administer the Krebiozen although it would have meant excessive travel. I declined on the grounds that I felt I would be prejudiced and that the former doctor would be better informed in its use as well as being more accessible. I am anxious to keep the doors open for more conventional treatment if, and when, the Krebiozen fails, and I hope it will not be too late then. I try to keep in touch with the family. However, I feel that we have all been rather lame in our not being able to present a more conclusive viewpoint and resolve all this ceaseless travel and turmoil."

From a doctor's letter to the editor.

Cleveland Clinic Foundation, Cleveland, Ohio. Inset: Rupert B. Turnbull, Jr., M.D.

Management of Occult Invasive Cancer in Polypoid Adenomas of the Colon and Rectum

The editor interviews Rupert B. Turnbull, Jr., M.D., The Cleveland Clinic Foundation, Cleveland, Ohio.

DR. GRANT: *Dr. Turnbull, because of the greater interest in carcinoma of the colon and rectum and the increasing use of the proctoscope, more and more polypoid adenomas of the colon and rectum are being found. What should be the treatment and management of the patient when a clinically benign adenomatous polyp is found?*

DR. TURNBULL: Our experience has given us support for recommending minimal surgical treatment in polypoid adenomas of the rectum.

DR. GRANT: *Is the treatment based upon the clinical appearance or determined by biopsy?*

DR. TURNBULL: Both of course, but it has been our observation that polypoid adenomas may be treated successfully by local measures even though foci of cancer are found on histological examination.

DR. GRANT: *Does this apply to all cases?*

DR. TURNBULL: Yes, but there are two requisites. First, the adenoma must appear clinically benign, that is, it must be flat or polypoid, freely movable, reasonably soft, and not ulcerated; and secondly, the adenoma must be destroyed completely to prevent local recurrence.

DR. GRANT: *Can you relate your experience which supports this treatment recommendation?*

DR. TURNBULL: Thirteen hundred and forty-five patients were studied to determine their survival following treatment of polypoid adenomas of the colon and rectum. Microscopic sections of the lesions were correlated with the clinical course. There were 117 (8.7%) polypoid adenomas with carcinoma in situ; 26 (2.0%) polypoid adenomas had carcinoma invading the lamina propria and were designated as superficial carcinoma. Thirty-seven (2.7%) adenomas had foci of invasive cancer. In these the cancer penetrated the muscularis mucosae but not the two principal muscular coats.

DR. GRANT: *Since all of these are very minimal cancers, strict selection must have been made.*

DR. TURNBULL: Oh, yes. Excluded from the study were all polypoid adenomas of patients with familial polyposis and those adenomas associated with cancer of the colon and rectum or found following resection for cancer and large villous adenomas.

DR. GRANT: *How were these patients treated?*

DR. TURNBULL: The adenomas were removed by local excision when they involved the colon and by biopsy and coagulation when they were situated in the rectum. Biopsy was made of the small rectal adenomas and the remaining portion coagulated to the base as an office procedure. The larger rectal adenomas were visualized and treated through the proctoscope by reducing their size piecemeal with biopsy forceps and then coagulating the residual base or stalk.

DR. GRANT: *What sort of results did you get with this type of treatment?*

DR. TURNBULL: The 37 patients having invasive cancer in the polypoid adenomas were followed to determine whether or not local recurrence of cancer or metastasis occurred. Thirty-one rectal adenomas were treated by coagulation and six colonic adenomas by transcolonic excision. All 37 patients were accounted for from four to 14 years after treatment. None died of cancer. One male, 77 years of age, had local recurrence of cancer in the rectum at the time of his death from a coronary occlusion, three years following repeated minimal coagulation. No patient died of metastasis. Two patients later developed new primary carcinomas of the rectum and colon, seven and 11 years after local treatment of the rectal adenomas containing foci of invasive cancer.

DR. GRANT: *Your experience convinces you that local treatment of cancer in benign-appearing polypoid adenomas is safe?*

DR. TURNBULL: Yes. The histologic finding of foci of invasive and noninvasive cancer has not altered our method of treatment, providing the adenoma has the appearance of a benign tumor to an experienced observer. This type of cancer apparently does not metastasize and, if adequately treated, does not recur locally.

Cancer of the Breast*

C. D. Haagensen, M.D.

The general practitioner, who must know much about many diseases, must certainly keep up with current thinking regarding cancer of the breast. One of every 20 of his women patients will sometime have this disease, one of every ten will come to him with some symptom referable to the breast.

The general practitioner, not the surgical specialist, sorts the patients, reassures those whose symptoms are due only to physiologic disturbance in the breast and sends those with signs of breast disease to a competent surgeon. The general practitioner thus bears the main responsibility for the clinical diagnosis of breast cancer.

There are three steps in this diagnosis:

1. The patient discovers a tumor in her breast and consults her physician.

2. The physician—usually the family doctor—examines the breast and makes a tentative clinical diagnosis. If he concludes that his patient has breast disease he refers her to a properly qualified surgeon.

3. The surgeon biopsies the tumor and proves its cancerous nature.

Any one of the three participants in this fateful drama of diagnosis may fail to do his duty and thus forfeit the chance of cure. This happens so often that in the average American community only about 50 percent of all patients with breast cancer have lesions that are still curable by operation when they reach the point at which a microscopic diagnosis has been made and treatment must be decided upon. *Our best hope for improving our results is to improve diagnosis.*

*Professor of Clinical Surgery, Columbia University College of Physicians and Surgeons, New York, N. Y.

*Reprinted by permission of World-Wide Abstracts 6:54-56, January, 1961.

The Patient

In the first of the three steps in diagnosis—the patient's perception of her breast tumor—nature has given women a great advantage. The breast is on the surface of the body and easily palpated. A cancer within it usually forms a definite tumor, distinguished from the surrounding softer breast tissue by its firmness, which most women feel perfectly well as something new and different. They may describe it as a "lump" or "thickening" or "hard knot." They usually discover it accidentally while bathing or dressing.

Some patients discover the tumor while it is as small as one centimeter in diameter—which proves that it is entirely possible for the perceptive patient to find her breast tumor while it is comparatively early and curable. The average patient coming to our clinic, however, has a tumor measuring more than five centimeters in diameter. From what we know of the rate of growth of breast cancer we can estimate that it takes from six to 12 months for a breast cancer to grow from a 1-cm size, at which it can be detected by careful palpation, to the 5-cm size at which we usually first see it.

Inquiry reveals that some women are indifferent to their breasts—they may be said not to be "breast-conscious." Naturally, such women are apt to discover a breast tumor later than those whose breasts are more important to them. When women do discover a breast tumor some are so frightened—for they share the common prejudice that all cancers are incurable — that they delay consulting a doctor for a long time. Whatever the cause of the

delay may be, it is astonishingly long. The average delay in my own series of private patients has been 7.5 months; and it has been 10.7 months in our ward patients. This fact seems almost unbelievable in a society in which education is generally available.

The other symptoms and signs of breast carcinoma—pain (which is infrequent), skin or nipple retraction, nipple discharge, nipple erosion, change in size or contour of the breast—are not often of importance in early recognition of breast disease by the patient. And early discovery by the patient must be our primary aim.

If breast cancer is to be detected the breasts must be examined at least every two or three months. Few women can manage to have a physician do this; there are not enough physicians, or enough time or money. Early detection can be achieved only by women examining their own breasts. Obviously they will do it better if they are taught how to do it. This was the purpose in making the film, "Breast Self-Examination," which has been widely shown by the American Cancer Society. In it I tried to demonstrate the method on which I myself rely in examining the breast, adapting it to subjective use. The patient lies supine with the side to be examined raised by a pillow under the shoulder. In this position the breast is balanced on the chest wall in as thin and even a layer as possible. In self-examination palpation is with the flat of the fingers of the patient's opposite hand. No effort is made to pick up the breast tissues between the fingers.

If self-examination is to be accepted, it is essential to convince women that it *can* be an accurate method of finding a breast tumor. In my own mind there is no doubt at all about this fact. As a specialist concentrating on finding breast disease I have been humbled often enough by a patient pointing out to me a small tumor that I had missed. This has taught me invariably to ask my patient where she feels a tumor if I have not found one. Women palpating their own breasts have the advantage of a proprioceptive tactile sense, and they are often very accurate. Even so, the alert woman who has been taught self-examination is apt to find her tumor earlier than the uninstructed woman. As proof of this fact I have in my case records a considerable number of patients who have come to me with very small breast carcinomas found by self-examination.

Self-examination is also likely to help calm the fear that keeps so many patients from consulting a physician for a long time after they have discovered a breast tumor. In becoming more familiar with their breasts, and through their confidence in the physician who has taught them self-examination, the problem of breast disease becomes much more matter-of-fact and so less frightening.

Some women are of course too jittery and hypochondriacal to attempt self-examination. They should be discouraged from attempting it.

The Family Physician

The second step in the diagnosis of breast disease is the examination carried out by the physician, usually the family doctor, when the patient comes to him with her breast tumor. Unfortunately, many physicians are neither methodical nor gentle in the examination. They usually examine the breasts with the patient sitting up, instead of in the supine position which I have recommended. They are often so heavy-handed that patients dread to return for examination.

Worst of all, they either fail to feel the tumor or procrastinate regarding

its significance in more than 20 percent of the patients who come to them with carcinoma. I do not make this statement lightly or without data to support it, and I am fully conscious of the fact that I myself have missed breast cancer. I am convinced from my own errors that the way to improvement in the clinical diagnosis of breast disease is to examine the breast more painstakingly and more gently with a methodical technique.

The examination begins with the patient sitting erect on the examining table with her feet over the side facing the physician, and in a good light. All clothes down to the level of the umbilicus have been removed. The examiner first palpates the axillas and the supraclavicular regions on each side. He then inspects the breasts, looking for changes in their size and contour, for deviation, retraction or erosion of the nipples, and most important of all, for skin retraction. The latter is often brought out by having the patient raise her arms above her head, by pectoral contraction with hands on the hips, or by the examiner gently lifting or molding the breast with his hand.

The patient is then asked to lie supine on the examining table. A small pillow is placed under the shoulder on the side of the breast to be examined and the arm is raised. The inner half of the breast is palpated first. Using the flat of the fingers of one hand, the examiner traces, so to speak, a series of transverse lines across the inner half of the breast, beginning in the infraclavicular region and proceeding caudad to the lower edge of the breast. He then follows the inframammary fold laterally to the lower outer sector of the breast.

The mammary tissue along the lower edge of the breast is often more dense and nodular than in other parts of the breast, forming, as it were, an inframammary ridge which should not be mistaken for disease. A tumor within this ridge stands out well enough, however, to be recognized as something abnormal.

The patient's arm is lowered to lie along her side, and the examiner palpates the outer half of the breast in a series of transverse lines beginning below and proceeding cephalad. The upper outer sector of the breast, where disease is most frequent, and where the breast is thicker and more difficult to examine, is palpated with extra care. Finally, the subareolar region is palpated. No attempt to express material from the nipple should be made.

If the examiner finds anything which he suspects represents disease in the breast there is a further maneuver that I recommend. It is the forward-bending maneuver. The patient stands erect and stretches out her hands to the examiner who sits in front of her. She then bends far forward while he supports her hands on his. In this position the normal breasts fall away from the body and are symmetrical. Any lesion causing fibrosis in the mammary tissue, such as carcinoma, produces skin retraction, or changes the contour of the breast, or if it involves the central corpus of mammary ducts, pulls in the nipple or deviates the axis in which it normally points. There are very few carcinomas that do not produce some type of retraction visible in this forward bending position. It has been of invaluable help to me in recognizing carcinoma of the breast.

From his initial or repeated examination the physician must shortly come to one of three conclusions:

1. *That his patient's breasts are normal*, and she need not return for special examination of the breasts.

2. *That her breast pain and in-*

creased nodularity are of physiologic origin and no actual disease is present. The relationship of these harmless physiologic phenomena to the menstrual cycle should be explained to the patient. In so doing the physician should not use that popular word "mastitis." It is not only unscientific, but it misleads the patient into believing that she does indeed have breast disease and it frightens her. It is wise to ask the patients with symptoms of physiologic origin to return for reexamination in three months.

3. *That she has breast disease.* Rather than attempt to define its nature the general practitioner should at once refer such a patient to a fully qualified surgeon. He should not himself attempt biopsy, or aspiration, or any further type of diagnostic procedure. For one thing he cannot know enough about these techniques to use them safely, and what is more important, they should only be carried out in a hospital with all preparations made for any operation that may be indicated. Many lives have been lost by general practitioner surgeons attempting to treat breast tumors.

The Surgeon

The third step in the diagnosis of breast cancer is consultation with a surgeon, and biopsy. I have not found any other diagnostic procedures, such as transillumination of the breast or x-ray examination, to be of any practical value, and I do not employ them. I particularly warn against the microscopic study of smears of nipple secretions as advocated by Papanicolaou and some of his pupils. Because of special features of the breast epithelium these nipple smears are deceptive. They cannot be depended upon to give a definite diagnosis, and squeezing the breast and the nipple to obtain secretion may well spread breast cancer.

Here are a few simple rules that experience has taught me:

1. DO NOT draw any conclusion from examination of the breasts while they are engorged during the premenstrual and menstrual phases of the cycle. The increased density and nodularity of the mammary tissue at this time leads to mistaking these physiologic changes for disease, and to unnecessary operations.

2. BEWARE of regarding breast disease as inflammation, and treating it conservatively with local applications and antibiotics. Except in association with lactation, inflammation is so rare that lesions with signs of inflammation must always be biopsied.

3. IF IN DOUBT about the interpretation of the findings, reexamine in a week or two. But never dismiss the patient for a longer time until you have made a definite diagnosis.

4. DO NOT DISREGARD the possibility that a very small tumor which the patient says she has had for a long time may be a carcinoma. A sympathetic surgeon naturally wishes to avoid operation. He is tempted to assume that a five-millimeter tumor which his patient insists she has had for several years is surely benign. This is not a safe assumption. The surgeon must stick to the rule of prompt biopsy for every dominant tumor of the breast.

Exception to this last rule should be made for two types of lesions:

(a) A rounded, movable breast tumor developing under the age of 21 is almost always a benign adenofibroma and there is no urgency about biopsy and excision. When they are done the skin incision should not be a radial one —which produces a disfiguring scar— but a circumareolar incision or a curved incision following the skin lines.

(b) When a woman in whom previous operation or aspiration has established the presence of breast cysts develops a new tumor that has the character of a cyst, its nature must of course be proved. This should be done, however, by aspiration rather than operation. If fluid is withdrawn and the tumor disappears no operation is required. Repeated operation for cystic disease is unjustified unless the new tumor is solid or has some other feature suggesting carcinoma.

Biopsy is the final step in the diagnosis of breast carcinoma. I believe that incisional biopsy is the most reliable, and therefore the preferred, type of biopsy. After all preparations for a radical mastectomy have been completed, including a full discussion of this possibility with the patient, incisional biopsy is performed in the operating room under general anesthesia. Frozen section is a reliable method of studying the small wedge of the lesion that is excised. Needle or trochar biopsy is a more brutal and much less exact method of biopsy.

The breast should never be removed without microscopic proof of the nature of the lesion within it. In our laboratory at Columbia we do not know any breast lesions that we regard as precancerous. I therefore remove the breast only when I know that it contains a fully malignant lesion. Mastectomy is rarely if ever justified as a precautionary measure in cystic disease.

Announcement

The Inter-Society Cytology Council will hold its annual meeting in Memphis, Tennessee, on November 2, 3, and 4. Additional information may be obtained by writing to: Dr. Paul A. Younge, Secretary-Treasurer, Inter-Society Cytology Council, 1101 Beacon Street, Brookline 46, Massachusetts.

"Until a better method of treating cancer of the stomach is discovered to supplant surgery, the most fertile field for improving our end results lies in the removal of all ulcerating lesions of the stomach regardless of how innocent they appear to be."

WHO: **Dr. J. E. Strode,** Department of Surgery, Straub Clinic, Honolulu, Hawaii.

WHERE: "Malignant Lesions of the Stomach in Hawaii: Experience with 350 Patients." *Surgery* 49:573-584, May, 1961; p. 583.

"In the absence of a magic cure-all for cancer, the best that can be done is to detect the disease as early as possible and treat it by the means available, namely surgery, irradiation or both. . . . Gynecologists have an exceptional opportunity to detect the major pelvic malignancy, cervical cancer, because it is essentially a lesion of the exterior of the body. . . . Thus, we have a great advantage over those physicians who are attempting to detect early malignancy of the internal organs."

WHO: **Dr. R. W. TeLinde,** Emeritus Professor of Gynecology, The Johns Hopkins University School of Medicine, Baltimore, Maryland.

WHERE: "Carcinoma In Situ of the Cervix." *Postgraduate Medicine* 29:458-464, May, 1961; p. 458.

"From the point of view of preventive medicine, if smoking leads to the development of even a single case of lung cancer, it is clearly the task of physicians and the tobacco industry to acknowledge this fact and to undertake steps to prevent such an occurrence."

WHO: **Dr. Ernest L. Wynder,** Associate Professor of Preventive Medicine, Sloan-Kettering Division of Cornell University Medical College.

WHERE: Boston, Massachusetts. November 18, 1960. New England States Chapter, American College of Chest Physicians.

"In those cases (exclusive of occult cancer) with multiple malignancy, the second cancer was more commonly responsible for death than the first cancer. To cure the first cancer and to allow the second cancer to become incurable while the patient is under observation is both embarrassing and tragic."

WHO: **Dr. John Pickren,** Chief of Pathology, Roswell Park Memorial Institute, Buffalo, New York.

WHERE: Manger Hotel. Rochester, N. Y. May 8-12, 1961. New York State Medical Society Meeting.

"It is now established beyond reasonable doubt that lung cancer would be reduced to less than 10 per cent of its present incidence if cigarette smoking were discontinued."

WHO: **Dr. Brian MacMahon,** Professor of Epidemiology, Harvard University School of Public Health.

WHERE: St. Petersburg, Florida. March 18, 1961. American Cancer Society's 1961 Science Writers' Seminar.

"For a breast lesion to increase in size from 1 to 2 cm in diameter, three doublings are required in the number of cells constituting the lesion. Since the mean doubling time for breast cancer lesions appears to be in the neighborhood of 90 days, it may be calculated that women presenting for mastectomy will usually have been bearing a detectable breast mass for a period of approximately 300 days or 10 months prior to time of radical mastectomy."

WHO: **Dr. Michael Brennan,** Director of Oncology, Henry Ford Hospital, Detroit, Michigan.

WHERE: Biltmore Hotel, New York, N. Y. June 1, 1961. Meeting of the American Cancer Society's Subcommittee on Breast Cancer.

"When one considers that most cancers of the thyroid develop in nontoxic goiters and that the thyroidectomy mortality in nontoxic cases is practically zero, the physician who advises a watchful waiting and 'do nothing' policy assumes a responsibility which he will find hard to justify. All too often in my own personal experience have I seen the tragic consequence of that unfortunate and misguided statement 'Don't bother it until it bothers you.'"

WHO: **Dr. Robert W. Bartlett,** Associate Professor of Clinical Surgery, Washington University, St. Louis, Missouri.

WHERE: St. Louis, Missouri. October 31-November 3, 1960. Fifty-fourth Annual Meeting, Section on Surgery, Southern Medical Association.

CANCER AROUND THE WORLD

"Prophylactic oncological screening of the whole population has become a routine in the U.S.S.R." This remarkable statement opens the section on cancer in a pamphlet entitled Health Services in the USSR, published by the World Health Organization in Geneva in 1960. The cancer section goes on to state that more than 100 million people were screened for cancer during the years 1945 to 1957. Depending upon the regions and population groups involved, the case-finding rates vary from 1.1 to 1.7 per thousand persons examined. The screening examination is carried to the individual rather than the reverse. This makes it possible to examine the people at their places of work, consequently, the examination can be conducted more easily and more people can be examined.

The overall cancer problem in the U.S.S.R. is approached as follows:

1. Ninety-four oncological polyclinics and dispensaries are distributed throughout the U.S.S.R. for the purpose of detecting cancer as early as possible and to insure early treatment. These centers are coordinated through a central institute—The Herzen Oncological Research Institute in Moscow. (All cases of cancer in Russia must be registered and a copy of such notification forwarded to the Academy of Medical Sciences.)

2. Practical research on the problem of cancer in general and clinical research is conducted at the Herzen Institute—an institute of the U.S.S.R. Health Ministry. Two hundred and fifty beds, a laboratory, and facilities for biochemical, biological and pathophysiological investigation are available.

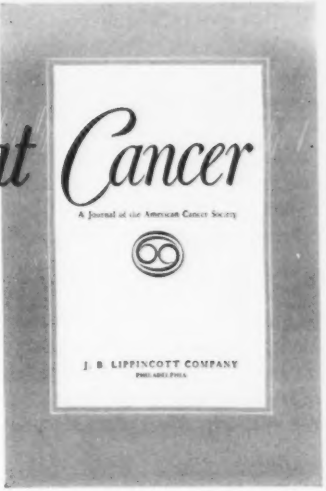
3. Pure cancer research is carried on in two institutes under the Academy of Medical Sciences. One is located in Moscow and the other in Leningrad.

Below is a table of cancer sites comparing the incidence in the U.S.S.R. and the U.S.A.

Type of Cancer	Percentage of All Cancer Cases	
	USSR	USA*
Stomach	33.0	5.6
Uterus and cervix	16.0	8.5
Skin	12.0	12.0
Other organs	10.0	45.2
Mouth	7.5	0.8
Lungs and bronchi	7.0	8.9
Breast	6.0	12.5
Esophagus	5.0	1.3
Rectum	2.0	3.9
Larynx	1.5	1.3
Total	100.0%	100.0%

**U.S.A. figures based on estimated incidence for 1960, compiled November, 1959. Since U.S. doctors are obliged to report only mortality data, rather than incidence data, some comparisons may not be reliable.*

Looking at Cancer



A commentary on the September-October, 1961 issue of CANCER, a journal of the American Cancer Society, Inc.

John W. Berg, M.D.
Associate Editor, Cancer

The life history of carcinoids, the most common neoplasms of the small intestine, is described by Moertel et al. While the majority of these tumors were silent and found incidentally at autopsy, about 25% were symptomatic and treated surgically. Any residual doubts concerning malignancy of these tumors vanishes with the observation that the metastatic rate was 86% in the symptomatic cases. It was a peculiar, indolent malignancy, however, for despite liver involvement in almost half the patients with metastases, the 5-year survival rate was 50%, and 27% of the patients with inoperable lesions survived five years! Preoperative diagnosis is difficult because of the varied and nonspecific symptoms. The carcinoid syndrome occurred in 7% of the patients; all but two of these 14 had liver metastases at the time.

A special difference in the personalities of cancer-bearing women and those with benign tumors is reported by Sugar and Watkins. They undertook to study women with breast tumors and the reasons for seeking or avoiding treatment. To eliminate the various alterations in psyche induced by mastectomy and the knowledge of serious disease, patients reporting a breast mass were interviewed before medical evaluation or biopsy. As expected more of the masses proved benign than malignant. Despite the time of the study, women with subsequently proven cancer were not like the patients with benign lesions. Both groups appeared fairly well aware of the danger of a breast lump. Patients with lesions later proven benign usually had become anxious when they found their masses and sought medical attention rapidly. On the other hand, patients with cancer tended to be depressed and in their depression denied the symptoms and significantly delayed consultation. Whatever the reason for this personality difference, one conclusion is of major importance: "... persons who are depressed or otherwise emotionally disturbed deny their troubles and mislead the physician. These individuals deserve

a further and fuller physical examination than do those who are not depressed . . ."

In a series of case illustrations Rothenberg describes the medical-emotional environment surrounding far advanced cancer patients. Too often these people are isolated and rejected even within hospital settings; they are too-vivid symbols of medical failure and impotence. On the wards the housestaff especially react in this way just when good rapport, understanding and support is most needed. It is often medical personnel insulation from fear and grief to treat diseases not patients but it is less than admirable medicine.

Public and professional education about cancer have produced quite tangible results in the practice of Anglem and Gray. After 1948 they began seeing earlier, smaller breast cancers with less axillary involvement than previously. Because of this and, so far as they can tell, because of this alone their 5-year survival has increased from 62% to 74%. They admit to limits on what standard surgery can accomplish but they deny that these limits have yet been reached.

The right of basal cell carcinomas to a malignant designation is supported by Cotran. He reports nine new cases of definite metastases from long-standing and stubborn but otherwise typical tumors. The frequency of metastasis in the Memorial Hospital material is estimated as 0.1%.

Takahashi studied esophageal carcinoma to determine what factors influenced the prognosis after surgery. Surprisingly, neither size, grade, nor presence of metastases was correlated with survival. More subtle histological changes were then tablulated. The single factor that proved of any value was the presence of a "host reaction," inflammation about the tumor.

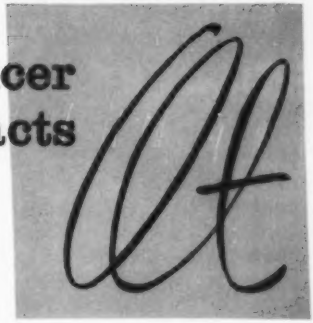
Shallow conization has been held to be less than optimal treatment for in situ cervix cancer. The danger of leaving gland ducts behind is pointed up by Voutsa and Foraker as they show by quantitative measurements that these ducts are the site of greater activity, atypia and anaplasia than the nearby surface epithelium.

Finding cancer cells in washings from operative wounds is not a guarantee of later wound recurrence. Arons and his coworkers in fact could find no correlation between positive washings and local recurrence or distant metastasis; neither was there a significant relation to survival even at five years.

The thrombogenic property of carcinoma of the body and tail of the pancreas is shown by Lafler and Hinerman to be due not to some special magic of the location but to the fact that a mixed duct-acinar type of cancer occurs there but not in the head of the pancreas.

Winkelmann by histochemistry adds further evidence that the so-called "juvenile melanomas" are far more like benign nevi than like true malignant melanomas.

cancer abstracts at a glance...



Lung Cancer Among the Indians

From 1954 to 1960, 50,000 chest X rays done on 8,287 adult Indians from the various reservations in California, Nevada, Arizona and Utah, revealed no cases of primary pulmonary cancer. There were two cases of metastatic lung disease. Dr. Samuel L. Cohen of the United States Public Health Service Indian Hospital interpreted all films.

The explanation of this absence of cancer of the lung is related to the fact that cigarette smoking is rare among Indians and there are no industrial fumes.

Previous reports by Smith and Kraus established a lowered morbidity and mortality of cancer especially among the Navajo and other Indian tribes of Arizona. This was found when all age groups were compared and hence could not be attributed to the lower life expectancy of the Indian.

Sievers, M. L., and Cohen, S. L.: Lung cancer among Indians of the southwestern United States. Ann. Int. Med. 54:912-915, May, 1961.

Practical Implications of Multiple Tumors of the Colon and Rectum

Patients with carcinoma of the colon or rectum should be divided into two groups: those with a solitary lesion; and those with one or more additional lesions, benign or malignant.

When one is dealing with a solitary malignant lesion of the colon or rectum the conventional type of resection appears to be indicated.

If either before or at the time of resection an additional tumor, benign or malignant, is found in the specimen, the amount of intestine removed should be extended beyond conventionally accepted limits.

For lesions of the ascending colon, the bowel should be resected to at least the left half of the mid-transverse colon. For lesions of the transverse colon, an ileosigmoidostomy should be performed. For lesions of the descending colon, an anastomosis between the left half of the mid-transverse colon and the rectosigmoid region should be carried out. For lesions of the rectum not amenable to restoration of continuity of the bowel, an extended Miles resection, with an end colostomy just distal to the splenic flexure, with mobilization of the latter, is indicated.

In addition to a more extensive initial operation, careful follow-up studies should be carried out at more frequent intervals in patients with more than one tumor of the colon.

—AUTHOR'S SUMMARY

Peabody, C. N., and Smithwick, R. H.: Practical implications of multiple tumors of the colon and rectum. New England J. Med. 264:853-855, April 27, 1961; p. 855.

FEEDBACK

TO THE EDITOR:

One of the real sources of pleasure and profit in reading *CA* is the aplomb with which differing and varying opinions are published in this valuable periodical. Sometimes even the facts on which opinions are based seem to be completely at variance.

An interesting example of this difference is embodied in your breezy compendium of quotes entitled "Now Hear This." In the Jan.-Feb. 1961 issue there is a speech dated Dec. 15, 1960 from a staff conference at Memorial Hospital at which Dr. Emerson Day of SKI-Cornell states "Eight of every nine detectable cancers of the rectum and colon will be missed if one depends on digital examination alone . . . "

The following issue (March-April) of "Now Hear This" refers to a speech, at Minneapolis, Minnesota, by Dr. Victor A. Gilbertsen "In our series of 501 patients with rectal cancer, virtually all of the lesions could be palpated by means of simple digital examination."

Since, presumably a figure of more than 500 patients with rectal cancer is a rather generous sample, we must conclude that somebody is statistically in error. At the moment the reader is left to choose between the incidence of one out of nine rectal cancers being detected by digital examination, or that "virtually all" rectal cancers can be palpated by simple digital examination. You pays your money, you takes your choice.

JOHN J. ANDUJAR, M. D.
Fort Worth Medical Laboratories
Forth Worth, Texas

TO THE EDITOR:

I am greatly disturbed by the implications of the statement of Dr. Victor A. Gilbertsen which appeared in "Now Hear This" in the March-April issue of *CA* (Vol. 11, No. 2, p. 69). It may well be true that "virtually all" of a large series of rectal cancers were palpable by simple digital examination, but this could apply only to bulky, fixed advanced lesions. Such are not the target of the cancer detection program of "earlier diagnosis for best prognosis."

In a series of 205 carcinomas of the rectum and colon diagnosed at Strang Clinic, Memorial Hospital, only 26 (12.7%) were within 8 cm of the anal margin. For detection of the remaining 179 (87.3%) proctosigmoidoscopy was obviously a requirement. Furthermore, in the experience of most of us, even many of the *early* lesions in the 1-8 cm rectal segment are first detected by visualization rather than by palpation because of their small size and lack of fixation.

The message which must be emphasized is that digital examination alone is *not* adequate for the detection of the majority of rectal cancers, and that the first localized and highly curable stages of cancer of both the rectum and the colon will be largely missed if we don't make a habit of insisting on proctosigmoidoscopy as well as digital examination.

EMERSON DAY, M. D.
Chairman,
Department of Preventive Medicine
Memorial Hospital for
Cancer and Allied Diseases

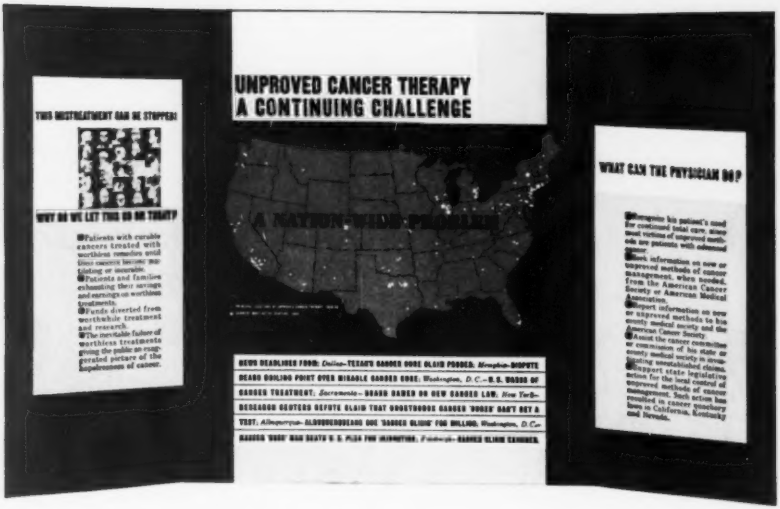
# of fishing and flowers

Cancer chemotherapy has been presented to the public and the Congress as holding great promise. The result has been a large federal-supported cancer chemotherapy testing program. This gigantic project was recently described by a British chemist as follows: "Three tumors are being used for testing thousands of drugs, and antibiotic brews submitted annually to this vast organization. While there is not basic objection to the philosophy of high sea net fishing, we, in Britain, do not wish to (and cannot) compete with this gargantuan setup. Our philosophy is based on the principle of fly fishing involving less man power, animals and cage space." High sea net fishing is producing some rather bizarre results and problems in cancer therapy. In some instances, it has brought reputable physicians to the very brink of quackery. At times it is difficult to determine whether a chemotherapeutic agent belongs in the same category as some rather obvious nostrums. The tragedy of the confusion arising from such uncertainty falls heaviest upon the cancer victim. The case report under the caption "From Pillar to Post" on p. 194 in this issue illustrates the type of misfortune which can befall such a patient.

There is, innately, within the field of cancer chemotherapy, the potential for easy misuse. Before one can establish himself as a surgical specialist in treating cancer, years of intensive training are necessary, and many requirements must be met, such as the approval of colleagues for hospital and operating room privileges. Similarly, the radiotherapist has to qualify himself through long years of training and must also have access to expensive, very complex hospital equipment. Such restrictions offer the cancer victim tremendous protection by eliminating self-styled cancer specialists in these fields. This does not exist, however, in chemotherapy. All the physician needs is a license to practice medicine and a chemical agent. Through publicity such an individual can become a world-renowned authority almost overnight, and attract cancer victims to his door from all parts of the country. It is so easy for questionable medical practices to spring up in chemotherapy that even with the best of intentions, it happens, when it delays the employment of established curative measures. For some inexplicable reason the cancer victim is particularly prone to exploitation, innocent or otherwise. Physicians in particular must be on guard to protect their cancer patients and to avoid participation in such practices:

"For sweetest things turn sour by
their deeds.
Lillies that fester smell far worse
than weeds."

Ruald M. Israel


THIS MISTREATMENT CAN BE STOPPED!
WHY DO WE LET THIS ON ON TODAY?
UNPROVED CANCER THERAPY
A CONTINUING CHALLENGE
WHAT CAN THE PHYSICIAN DO?

Unproved Cancer Therapy, A Continuing Challenge

Pictured above is an exhibit for the medical profession entitled, "Unproved Cancer Therapy, A Continuing Challenge," which is available on loan through the American Cancer Society Divisions.

The exhibit emphasizes that unproven cancer therapy is a continuing problem that plagues cancer victims throughout the entire United States. A map showing the principal locations of unproved cancer therapy activity in the past decade is the central feature. What physicians can do to help solve the problem are listed, the most important of which is support of state legislative action for control of unproven methods of cancer treatment. Such legislation has been enacted in California, Kentucky, Nevada and Colorado, and similar laws are to be encouraged for enactment in the remaining states in order that the problem can be controlled in the local community where the patient comes into contact with the unproven method.

There are two versions of the exhibit. One is 10 feet in diameter and suitable for state medical society meetings. The other is a 3' x 5' cardboard version which is suitable for staff and tumor conference rooms.